

## ORIGINAL ARTICLE

# Urinary Chloride-to-Creatinine Ratio as an Early Predictor of Diuretic Resistance in Acute Heart Failure

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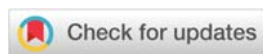
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## ABSTRACT

**Background:** Diuretic resistance is an important issue in the management of acute heart failure, as it is associated with slow decongestive response and high likelihood of ongoing fluid retention, renal failure and longer hospital stays. The aim of this study was to assess the usefulness of the urinary chloride to creatinine ratio as an early predictor for inadequate diuretic response.

**Methods:** This is a prospective, observational study of 110 adults hospitalized at Mayo Hospital Lahore with acute heart failure from April 2025 to April 2026. Spot urine was done two hours following the first dose of intravenous Furosemide. Diuretic resistance was considered to be low urine output on 24-hour basis, poor weight loss and intensification of diuretic therapy. ROC analysis and multivariable logistic regression were undertaken.

**Results:** Diuretic resistance occurred in 35 patients (31.8%). The median urinary chloride to creatinine ratio was significantly lower in resistant compared to responsive patients (56 [38-72] vs 118 [86-156] mmol/g,  $p < 0.001$ ). A cut-off of  $< 72$  mmol/g was shown to have 82.9% sensitivity, 78.7% specificity, and an area under the curve of 0.86 for predicting resistance. A ratio  $< 72$  mmol/g was independently associated with resistance after the adjustment (adjusted odds ratio 6.18; 95% confidence interval 2.43–15.69;  $p < 0.001$ ). Resistant patients were also less likely to have high urine output, less net fluid loss, more worsening renal function, persistent congestion, and shorter hospital stay. After adjustment for kidney function, systolic blood pressure, chronic use of a loop diuretic, serum chloride and sex, the association was still present, suggesting that it is independently predictive in routine clinical practice settings.

**Conclusion:** Urinary chloride to creatinine ratio is a fast, simple, and clinically helpful method of rapid assessment of early diuretic resistance in acute heart failure.

**Keywords:** acute heart failure; chloride; creatinine; decongestion; diuretic resistance; furosemide; urinary biomarkers

## INTRODUCTION

Acute heart failure is a common cause of emergency hospitalisation and often associated with pulmonary or

systemic congestion<sup>1</sup>. Intravenous loop diuretics are the primary therapy for fluid overload to help decrease filling pressures, dyspnea and restore functional status. But there

is great individual variation in the response to loop-diuretic therapy. Some people achieve immediate natriuresis and good decongestion while others have poor urine production and ongoing congestion despite apparently good doses. This is a decreased responsiveness and is often termed “diuretic resistance”<sup>2</sup>.

Diuretic resistance is clinically important as it is associated with prolonged hospitalisation, increased treatment complexity, worsening renal function, residual congestion and increased risk of early readmission<sup>3</sup>. It is multifactorial in its development, including sub-optimal renal perfusion, decreased diuretic delivery to the tubular lumen, neurohormonal activation, chronic kidney disease, distal nephron adaptation, increased sodium reabsorption, and prior exposure to high dose loop diuretics. Patients at risk can be identified early and allow for timely dose adjustment, sequential nephron blockade and closer monitoring prior to the onset of overt treatment failure<sup>4</sup>.

The diuretic response is generally evaluated by urine output, daily weight gain/loss, fluid balance, clinical evaluation, and changes in renal function<sup>5</sup>. These measures are helpful but might not give adequate early information. There may be fluctuations in body weight from measurement, fluid intake and changes from non-fluid causes and clinical signs of congestion may be slow to improve. Urinary output can also be misleading as it is not necessarily equivalent to excretion of sodium and chloride. Hence, the interest in simple urinary markers that can give a quick and objective measurement of the renal response to loop diuretics therapy<sup>6</sup>.

The natriuretic response has been extensively studied by measuring urinary sodium<sup>7</sup>. However, spot urinary electrolyte concentrations depend on the degree of urine dilution, the time of collection, diet, renal function and other medications. Low electrolyte concentration can be due to poor tubular excretion or highly diluted urine. This limitation can be reduced by normalization for urinary creatinine, which will adjust the electrolyte concentration for changes in the urine concentration<sup>8</sup>.

In acute heart failure, chloride may be of particular interest as it has a key role in renal sodium handling, tubuloglomerular feedback and neurohormonal regulation<sup>9</sup>. A decreased urinary chloride indicates continued reabsorption of chloride and failure of blockade of sodium-chloride reabsorption. It could then represent a physiological condition, where the kidney is still not receptive to decongestive therapy. The urinary chloride-to-creatinine ratio may be a more stable measurement of chloride excretion since it is not affected by differences in urinary concentrations<sup>10</sup>.

Although this ratio may be clinically useful, it has not been well determined as an early predictor of resistance to diuretics<sup>11</sup>. An easily accessible and available marker within

the first few hours of therapy could identify patients unlikely to achieve a sufficient response to the initial diuretic therapy. To this end, the present study was designed to assess the urinary chloride-to-creatinine (UCCR) ratio after a bolus of intravenous loop-diuretics, and to investigate if this ratio could predict diuretic resistance in hospitalised patients with acute heart failure (AHF)<sup>12</sup>.

## MATERIALS AND METHODS

**Study Design and Setting:** A one-year (April 1, 2025, to April 1, 2026) prospective observational cohort study was carried out in the Department of Cardiology of the tertiary care hospitals of Punjab. The study examined the validity of urinary chloride-to-creatinine ratio measured soon after intravenous loop diuretic therapy for predicting diuretic resistance in the acute hospital setting in patients with acute heart failure.

**Study Population:** One hundred and ten (110) cases of consecutive patients at Mayo Hospital Lahore with acute heart failure with clinical evidence of fluid congestion were sampled using a non-probability consecutive sampling technique. Acute heart failure was assessed by the presence of consistent symptoms, physical examination findings, cardiac imaging, chest radiography findings and elevated natriuretic peptide concentrations (where available).

**Inclusion Criteria:** Patients  $\geq 18$  years old were eligible if they had primary acute heart failure diagnosis, received intravenous loop diuretic therapy, and exhibited  $\geq 2$  clinical signs of congestion. These features were pulmonary crackles, peripheral edema, elevated jugular venous pressure, ascites, pulmonary congestion on chest radiograph or inferior vena cava dilatation.

**Exclusion Criteria:** Patients were excluded when the following conditions occurred: cardiogenic shock, acute coronary syndrome with urgent revascularization, maintenance dialysis, estimated glomerular filtration rate (eGFR)  $<15$  mL/min/1.73 m<sup>2</sup>, anuria, urinary tract obstruction, active urinary tract infection, nephrotic syndrome, advanced chronic liver disease, and incomplete urine collection. Patients who had been given intravenous loop diuretics within 2 hours of enlistment or intravenous contrast within 24 hours before enlistment were also excluded.

**Ethical Considerations:** The Study was approved by the Institutional Review Board. All subjects read and understood the purpose and procedure of the study and signed informed consent before entering the study. Patient

data was coded and kept confidential during the entire study.

**Baseline Clinical Assessment:** Demographic data, comorbidities, prior hospitalizations for heart failure, and chronic medications, including pre-admission loop diuretic doses were collected on a structured data collection form. Body weight, blood pressure, heart rate, oxygen saturation, jugular venous pressure, pulmonary crackles and peripheral oedema were measured at baseline.

Laboratory tests requested were complete blood count, sodium, potassium, chloride, bicarbonate, urea, creatinine, albumin and (where available) B-type natriuretic peptide. Serum creatinine was used for estimated glomerular filtration rate. Transthoracic echocardiography was done during the admission or within 3 months prior to admission and left ventricular ejection fraction was recorded.

**Initial Diuretic Treatment:** Patients not on chronic loop diuretic therapy received intravenous furosemide 40-80mg depending on congestion severity and renal function. The initial intravenous dose of diuretic was an amount of furosemide equivalent to or at least as great as the total daily oral dose given to the patient already receiving an oral loop diuretic.

Oral loop-diuretic doses were translated to furosemide equivalents; an oral dose of 40 mg furosemide was deemed to be approximately equivalent to an oral dose of 20 mg torsemide and 1 mg bumetanide. Additional diuretic therapy was left to the discretion of the attending cardiologist based on urine output, clinical findings, blood pressure, renal function and electrolyte levels.

**Urine Collection & Laboratory Measurement:** If possible, the urinary bladder was emptied immediately prior to the intravenous administration of furosemide. Two hours following the first intravenous dose, a spot urine was obtained. Sample was promptly sent to a hospital laboratory to have chloride and urinary creatinine levels measured.

Urinary chloride was analysed by ion-selective electrode method while urinary creatinine was analysed by enzymatic or compensated Jaffé method available in the institutional laboratory. Laboratory staff had no knowledge of the subsequent classification of diuretic response.

**Urinary chloride to creatinine ratio was determined by the following formula:**

Chloride-to-creatinine ratio in urine = urinary chloride (mmol/L) / urinary creatinine (g/L).

This ratio was reported in units of mmol of chloride/gram of urinary creatinine.

**To Evaluate Diuretic Response:** Urine output was measured over the next six hours after drug administration and over 24 hours after drug administration. Fluid intake, net fluid balance, daily body weight, total intravenous diuretic dose and need of extra diuretic agents were recorded.

Diuretic resistance for the first 24 hours was the primary outcome. Diuretic resistance was considered to be a 24-hour urine output of less than 1,500 mL and a loss of less than 0.5 kg of body weight despite receiving at least 80 mg of intravenous furosemide equivalent or at least twice the patient's usual daily dose of oral loop diuretics.

Patients who needed early use of a thiazide or thiazide-like diuretic because of persistent congestion and inadequate urine output were also considered to have diuretic resistance.

**Secondary Outcomes:** Six-hour urine output, 24-hour urine output, net fluid loss, change in body weight, total intravenous furosemide requirement, worsening renal function, residual congestion at discharge, hospital length of stay, intensive care unit admission and in-hospital mortality were secondary outcomes.

A rise in serum creatinine of  $\geq 0.3$  mg/dl from baseline within 72 hours was considered worsening renal function. Residual congestion was deemed to exist if 2 or more signs of congestion were found at discharge.

**Statistical Analysis:** IBM SPSS Statistics 27.0 software was used to enter and analyze data. Normality was checked for continuous variables and presented as mean and standard deviation or median and interquartile range. Categorical data were presented in frequencies and percentages.

Patients were categorised as diuretic-resistant and diuretic-responsive. Independent-samples t test or Mann-Whitney U test was used to compare continuous variables and chi-square test or Fisher exact test was used to compare categorical variables.

Spearman correlation analysis was used to assess relationships between the urinary chloride-to-creatinine ratio and urine output, net fluid loss, weight loss and total loop-diuretic dose. Receiver-operating-characteristic curve analysis was used to determine the ability of the ratio to predict diuretic resistance. The best cut-off value was determined by the Youden index and the sensitivity, specificity, positive predictive value and negative predictive value were calculated.

All variables with a p value < 0.10 in the univariable logistic regression analysis were included in a multivariable analysis, along with clinically relevant variables. Adjusted odds ratios (AOR) were presented with 95% confidence intervals (CI). Statistically significant p value was set as < 0.05 (two sided).

## RESULTS

A total of 110 patients with acute heart failure were enrolled. Their mean age was  $66.9 \pm 11.4$  years, and the cohort comprised 66 men (60.0%) and 44 women (40.0%). 35 patients (31.8%) became resistant to diuretics, while 75 patients (68.2%) responded well. There were 20 men and 15 women in the resistant group and 46 men and 29 women in the responsive group. There was no significant difference between the groups in terms of sex distribution.

Patients who were diuretic resistant had more prevalent chronic kidney disease, prior hospitalizations for heart failure, and chronic use of loop diuretics. They also exhibited a lower serum chloride concentration and higher B-type natriuretic peptide concentration, a lower estimated glomerular filtration rate and a lower systolic blood pressure. Table 1 demonstrates that no differences existed between the groups in terms of age, sex, diabetes, hypertension, atrial fibrillation, or left ventricular ejection fraction.

Patients with diuretic resistance had significantly reduced 2 hour urinary chloride and sodium levels. Urinary chloride to creatinine ratio was significantly lower in patients with resistance to thiazide, whereas urinary creatinine concentration was similar in both groups.

The urine output at 6 and 24 hours, the net fluid loss, the body-weight reduction, and the cumulative dose of intravenous furosemide were also lower in patients with resistance. The chloride to creatinine ratio of the urine was found to be positively correlated with six-hour urine output, 24-hour urine output and net fluid loss. This was negatively correlated with the total furosemide requirement.

ROC analysis revealed that urinary chloride:creatinine ratio had an AUC of 0.86 for prediction of resistance. The cut-off value of  $< 72$  mmol/g had a sensitivity of 82.9%, specificity of 78.7%, positive predictive value of 64.4%, and a negative predictive value of 90.8%. The urinary and decongestive results are given in Table 2.

**Table 1:** Baseline characteristics according to diuretic response

| Characteristic                          | Diuretic resistance (n=35) | Adequate response (n=75) | p value |
|-----------------------------------------|----------------------------|--------------------------|---------|
| Age, years                              | $69.2 \pm 10.4$            | $65.8 \pm 11.7$          | 0.143   |
| Male patients, n (%)                    | 20 (57.1)                  | 46 (61.3)                | 0.676   |
| Female patients, n (%)                  | 15 (42.9)                  | 29 (38.7)                | 0.676   |
| Diabetes mellitus, n (%)                | 22 (62.9)                  | 34 (45.3)                | 0.087   |
| Hypertension, n (%)                     | 28 (80.0)                  | 56 (74.7)                | 0.540   |
| Chronic kidney disease, n (%)           | 16 (45.7)                  | 15 (20.0)                | 0.005   |
| Atrial fibrillation, n (%)              | 14 (40.0)                  | 25 (33.3)                | 0.494   |
| Previous heart-failure admission, n (%) | 28 (80.0)                  | 44 (58.7)                | 0.028   |
| Chronic loop-diuretic use, n (%)        | 30 (85.7)                  | 46 (61.3)                | 0.010   |
| Systolic blood pressure, mmHg           | $117 \pm 18$               | $126 \pm 21$             | 0.034   |
| Left ventricular ejection fraction, %   | $36 \pm 12$                | $39 \pm 14$              | 0.279   |
| Serum creatinine, mg/dL                 | 1.55 (1.20–1.91)           | 1.12 (0.90–1.43)         | <0.001  |
| eGFR, mL/min/1.73 m <sup>2</sup>        | $46 \pm 18$                | $65 \pm 22$              | <0.001  |
| Serum chloride, mmol/L                  | $97.8 \pm 4.7$             | $101.0 \pm 4.9$          | 0.002   |
| BNP, pg/mL                              | 1,420 (920–2,210)          | 960 (590–1,580)          | 0.006   |
| Initial intravenous furosemide dose, mg | 80 (60–100)                | 60 (40–80)               | 0.018   |

**Table 2:** Urinary biomarkers, decongestive response, and predictive performance

| Variable                                      | Diuretic resistance (n=35) | Adequate response (n=75) | p value |
|-----------------------------------------------|----------------------------|--------------------------|---------|
| Two-hour urinary chloride, mmol/L             | 42 (28–57)                 | 85 (63–110)              | <0.001  |
| Two-hour urinary sodium, mmol/L               | 45 (30–61)                 | 86 (62–112)              | <0.001  |
| Two-hour urinary creatinine, g/L              | 0.76 (0.52–1.05)           | 0.73 (0.50–1.00)         | 0.581   |
| Urinary chloride-to-creatinine ratio, mmol/g  | 56 (38–72)                 | 118 (86–156)             | <0.001  |
| Six-hour urine output, mL                     | 620 (460–790)              | 1,230 (950–1,570)        | <0.001  |
| Twenty-four-hour urine output, mL             | 1,220 (980–1,430)          | 2,780 (2,250–3,440)      | <0.001  |
| Twenty-four-hour net fluid loss, mL           | 1,090 (700–1,400)          | 2,470 (1,880–3,060)      | <0.001  |
| Twenty-four-hour weight change, kg            | –0.3 (–0.5 to 0.0)         | –1.2 (–1.7 to –0.8)      | <0.001  |
| Total 24-hour intravenous furosemide dose, mg | 160 (120–200)              | 100 (80–140)             | <0.001  |
| Additional thiazide-type diuretic, n (%)      | 17 (48.6)                  | 8 (10.7)                 | <0.001  |
| AUC for urinary chloride-to-creatinine ratio  | 0.86                       | 0.79–0.92                | <0.001  |
| Optimal cutoff                                | <72 mmol/g                 | —                        | —       |
| Sensitivity                                   | 82.9%                      | —                        | —       |
| Specificity                                   | 78.7%                      | —                        | —       |
| Positive predictive value                     | 64.4%                      | —                        | —       |
| Negative predictive value                     | 90.8%                      | —                        | —       |

**Table 3:** Independent predictors and in-hospital outcomes

| Variable                                               | Adjusted odds ratio        | 95% confidence interval  | p value |
|--------------------------------------------------------|----------------------------|--------------------------|---------|
| Urinary chloride-to-creatinine ratio <72 mmol/g        | 6.18                       | 2.43–15.69               | <0.001  |
| eGFR, per 10 mL/min/1.73 m <sup>2</sup> increase       | 0.79                       | 0.65–0.96                | 0.017   |
| Chronic furosemide-equivalent dose, per 40 mg increase | 1.37                       | 1.04–1.81                | 0.026   |
| Systolic blood pressure, per 10 mmHg increase          | 0.83                       | 0.69–0.99                | 0.043   |
| Serum chloride, per 1 mmol/L increase                  | 0.93                       | 0.85–1.01                | 0.081   |
| Female sex                                             | 1.12                       | 0.45–2.79                | 0.807   |
| Clinical outcome                                       | Diuretic resistance (n=35) | Adequate response (n=75) | p value |
| Worsening renal function, n (%)                        | 13 (37.1)                  | 11 (14.7)                | 0.008   |
| Residual congestion at discharge, n (%)                | 15 (42.9)                  | 10 (13.3)                | 0.001   |
| Length of hospital stay, days                          | 8 (6–10)                   | 5 (4–7)                  | <0.001  |
| Intensive care unit admission, n (%)                   | 7 (20.0)                   | 5 (6.7)                  | 0.037   |
| In-hospital mortality, n (%)                           | 3 (8.6)                    | 2 (2.7)                  | 0.166   |

In multivariable logistic regression, a urinary chloride-to-creatinine ratio below 72 mmol/g remained the strongest independent predictor of diuretic resistance. Lower estimated glomerular filtration rate, higher chronic loop-diuretic exposure, and lower systolic blood pressure were also independently associated with resistance. Female sex was not associated with the outcome.

Patients with resistance had higher rates of worsening renal function, residual congestion, intensive care admission, and longer hospitalization. In-hospital mortality was numerically higher in the resistant group but did not reach statistical significance. The adjusted predictors and clinical outcomes are presented in Table 3.

Generally, the low two-hour urinary chloride-to-creatinine ratio was linked to low urine output, poor decongestion, high diuretic needs and poor in-hospital outcomes. This association was also present when the investigators adjusted for sex, kidney function, blood pressure, and prior diuretic use.

## DISCUSSION

The present study evaluated the urinary chloride-to-creatinine ratio as an early marker of diuretic resistance in patients hospitalized with acute heart failure<sup>1</sup>. The key discovery was that urinary chloride-to-creatinine ratio was significantly decreased 2 hours after intravenous furosemide in patients who developed diuretic resistance. A ratio of less than 72 mmol/g showed good discriminatory ability and was independently associated with resistance even after accounting for renal function, BP, chronic loop-diuretic use, serum chloride and sex<sup>2</sup>.

About 33% of subjects in the study were diuretic resistant<sup>3</sup>. Such patients had a decreased 6-hour and 24-hour urine output, decreased net fluid loss, minimal decrease in body weight, and a higher need for intravenous furosemide and extra thiazide treatment. The present data show that the initial urinary chloride/creatinine ratio was not only a good indicator of the initial renal response to loop diuretic administration but also was a good indicator

of the effectiveness of decongestion over the following 24 hours<sup>4</sup>.

Loop diuretics inhibit the reabsorption of sodium and chloride in the thick ascending limb of the loop of Henle<sup>5</sup>. A good response should therefore result in rapid urinary chloride excretion, as well as natriuresis and diuresis. Low urinary chloride-to-creatinine ratio can be due to poor delivery of the diuretic to the site of its action, poor renal perfusion, greater neurohormonal activation, or greater compensatory chloride reabsorption in distal nephron segments. These mechanisms may all play a role in causing persistent fluid retention in the face of escalating doses of diuretic treatment<sup>6</sup>.

Using urinary creatinine as the denominator may help to interpret spot urine chloride measurements<sup>7</sup>. Urine dilution, volume intake and timing of urine collection all influence the absolute chloride content of urine. Some of this variability can be accommodated by adjusting for urinary creatinine, which may give a more stable estimate of chloride excretion. In the current study, urinary creatinine levels were comparable between the resistant and responsive groups while the chloride to creatine ratio was significantly different, suggesting that the difference was mainly due to reduced chloride excretion<sup>8</sup>.

The ROC curve of the ratio showed good prediction with an area under the curve of 0.86<sup>9</sup>. What was noteworthy was its negative predictive value of 90.8%. This indicates that patients with ratio  $\geq 72$  mmol/g were less likely to develop early diuretic resistance. Clinically, this could help to reassure the clinician that the initial loop diuretic treatment is having an acceptable effect on the kidneys, and that a lower ratio might indicate that a treatment target should be sought at an earlier stage in treatment<sup>10</sup>.

The urinary chloride-to-creatinine ratio < 72 mmol/g was more than six times more likely to be associated with diuretic resistance<sup>11</sup>. This association was retained after adjusting for a number of known clinical factors associated with inadequate diuretic response. An additional independent predictor of resistance was reduced

estimated glomerular filtration rate. Decreased renal delivery of the loop diuretics and decreased filtered sodium and chloride load to be excreted may be present. Another independent predictor was exposure to loop diuretics for a long period of time, possibly due to adaptation of the distal tube and reabsorption of more sodium-chloride after long-term treatment<sup>12</sup>.

A decrease in systolic blood pressure was correlated with a decrease in diuretic response<sup>13</sup>. Those patients with lower blood pressures may have poor renal perfusion and limited ability to tolerate more aggressive diuresis. In the unadjusted analysis, resistant patients had lower serum chloride levels, which were not statistically significant in the multivariable analysis. This implies that the urinary chloride handling following a diuretic treatment might be more useful as a immediate indicator of response to treatment than the chloride concentration in the blood alone<sup>14</sup>.

Male and female patients were included in the study without regard to sex, and sex alone was not a significant determinant of diuretic resistance<sup>15</sup>. This imbalance in the sex distribution in the study did not account for the predictive association of the urinary chloride-to-creatinine ratio. This is encouraging in terms of the marker's potential to be applicable to both male and female acute heart failure patients<sup>16</sup>.

Patients who were diuretic resistant had higher incidences of worsening renal function, residual congestion, intensive care unit admission and longer hospital stays<sup>17</sup>. These negative effects were in line with the decrease in urinary output and insufficient fluid removal in the first 24 hours. There were numerically more in-hospital deaths in the resistant group, but this was not statistically significant, which may be due to the low death rate and low numbers of patients<sup>18</sup>.

The chloride-to-creatinine ratio of urine has several potential clinical benefits<sup>19</sup>. It can be determined from a single spot urine sample, requires routinely performed lab tests, and is known within a few hours of treatment. If it is recognized early that response is poor, it may be possible to increase the dose of the loop diuretic, evaluate delivery or compliance with the drug, institute sequential nephron blockade, or more closely monitor renal function and electrolyte disorders<sup>20</sup>.

The ratio should not, however, be used as a treatment target alone<sup>6</sup>. Factors affecting diuretic response include renal function, haemodynamic status, prior exposure to drugs, dietary sodium intake, venous congestion and severity of cardiac dysfunction. Therefore, it is important to consider the urinary ratio in conjunction with urine output, blood pressure, serum electrolytes, renal function, body weight and clinical evidence of congestion<sup>13</sup>.

There were some weaknesses in this study<sup>3</sup>. It was done at one center with a relatively small sample size, limiting the applicability of the results. Diuretic resistance was defined as a combination of urine output, body-weight change, amount of diuretic used and the need for other therapy; a definition now does not exist<sup>17</sup>.

Urinary chloride to creatinine ratio was only evaluated at one time point<sup>8</sup>. Longitudinal measurements may give more detailed data of the renal chloride handling changes during treatment. Muscle mass, sex, nutritional status, kidney function and age are also factors affecting urinary creatinine. A 24-hour urinary chloride excretion was not collected, so it was not possible to directly compare the spot ratio with the chloride excreted over the 24 hours<sup>15</sup>.

The attending physicians made the decision for treatment without taking the urinary ratio into account<sup>9</sup>. Hence, the study showed predictive association only, and not if the ratio-guided therapy is beneficial for decongestion or for clinical outcomes. The proposed cut-off needs to be confirmed by larger multicenter studies, and its value in treatment guided protocols should be assessed<sup>19</sup>.

## CONCLUSION

Two-hour post-furosemide urinary chloride-to-creatinine ratio was a good predictor of diuretic resistance in acute heart failure patients. A threshold of <72 mmol/g was associated with lower urine output, less net fluid loss, higher diuretic dose, persistent congestion, and poorer renal function, and longer hospital stay.

Even when kidney function, blood pressure, chronic diuretic use, serum chloride, and sex were factored in, the ratio was still an independent predictor. The urinary chloride-to-creatinine ratio might be a convenient screening tool for insufficient decongestive response as it can be obtained quickly from a routine spot urine sample. The cutoff should be validated in multicenter prospective studies to see if the ratio can be used to enhance patient outcomes when incorporated into diuretic-management strategies.

## DECLARATION

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**Data Availability Statement:** The data that supports the findings of this research are available on request from Corresponding Author.

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