

### Background

There have been few studies on the relationship between serum chloride concentration and patients' prognosis in the Emergency Department(ED), diagnosed with septic shock. We hypothesized that higher chloride levels of patients with severe sepsis or septic shock are associated with higher mortality rates.

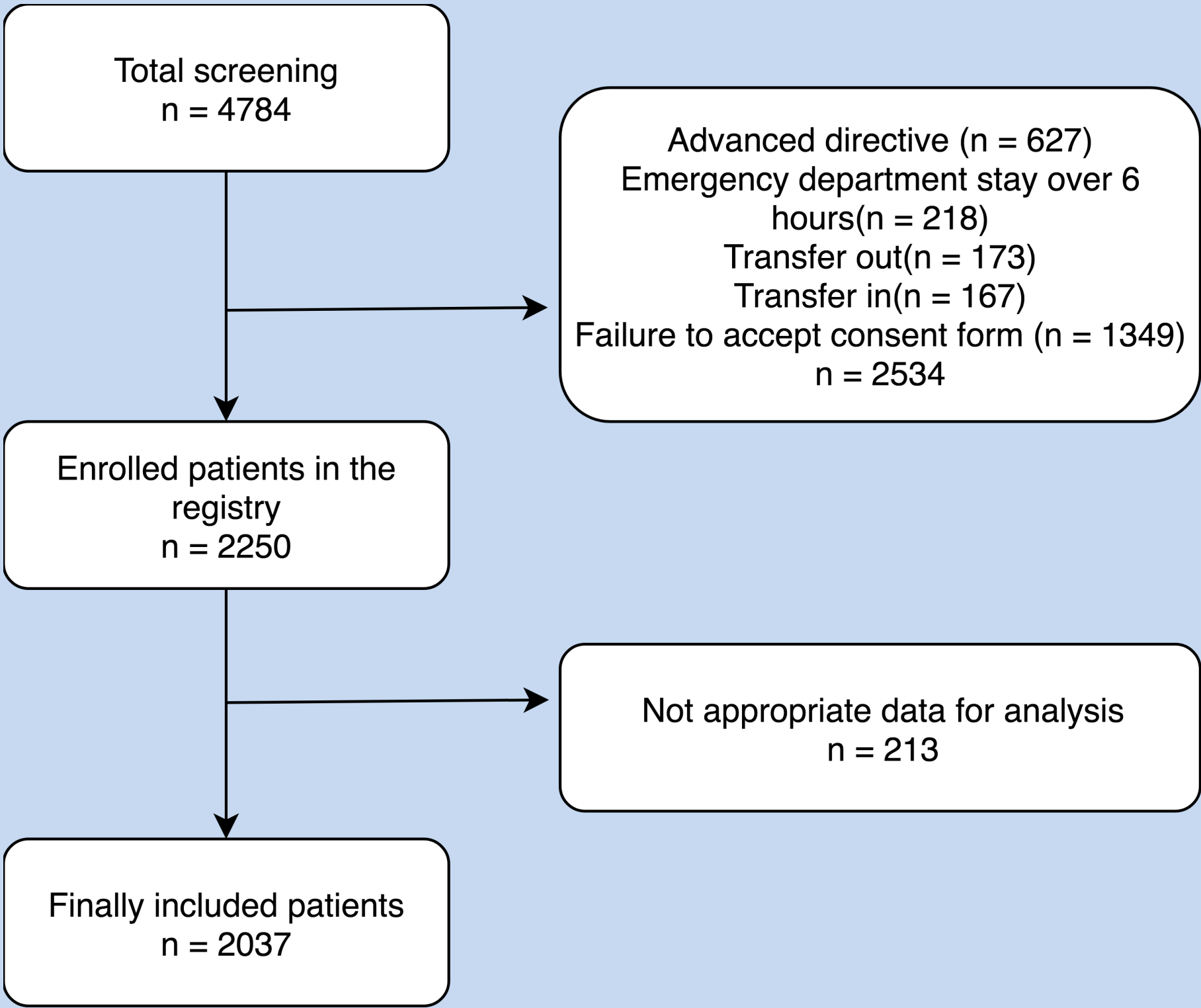
### Patients & Methods

This retrospective observational study used data from a prospectively-collected multicenter ED based registry of the Korean Shock Society (KoSS), between October 2015 and April 2018. 21 tertiary level EDs were participated. The primary outcome was 28-day mortality rate .

### Data collection

A case report form of the KoSS septic shock registry takes in standard definitions of 200 variables including baseline characteristics, co-morbidities, therapeutic interventions and outcomes of septic shock patients.

Figure 1. Patient flow diagram



### Results & Discussion

Patients were divided into three groups according to the initial serum chloride concentration:

Hypochloremia < 98 mEq/L  
Normochloremia 98-110mEq/L  
Hyperchloremia > 110 mEq/L

The 28-day mortality rate was most highly reported in hyperchloremic group.

hypochloremia vs. normal vs. hyperchloremia  
23.8% vs. 19.2% vs. 34.7%, P-value < 0.001

After adjusted for confounding variables in multivariate logistic regression analysis; age, gender, acid-base state, SOFA score, and lactate levels, the 28-day mortality risk was significantly increased in hyperchloremic group (Adjusted OR 1.65, 95% CI 1.0-2.7; P-value 0.04) and hypochloremia group (Adjusted OR 1.3, 95% CI 1.02-1.67; P-value 0.04).

Subgroup analysis was performed by the acid-base state. Adjusted ORs for 28-day mortality was significantly increased in the hypochloremia group(Adjusted OR 1.84 95% CI 1.13-3.01; P-value 0.01) but not in the hyperchloremia group (Adjusted OR 1.08, 95% CI 0.49-2.39; P-value 0.85).

### Conclusion & Perspectives

We found out that hypochloremia is a fatal risk factor for severe sepsis or septic shock patients, even after adjusting for confounders. Subgroup analysis also revealed that hypochloremia is a significant risk factor, especially in the septic shock patient with acidosis. It can be explained considering the fact that hypochloremia induces metabolic alkalosis to compensate for the acidic state such as lactic acidosis.

Figure 2. Main results of multivariable logistic regression analysis.

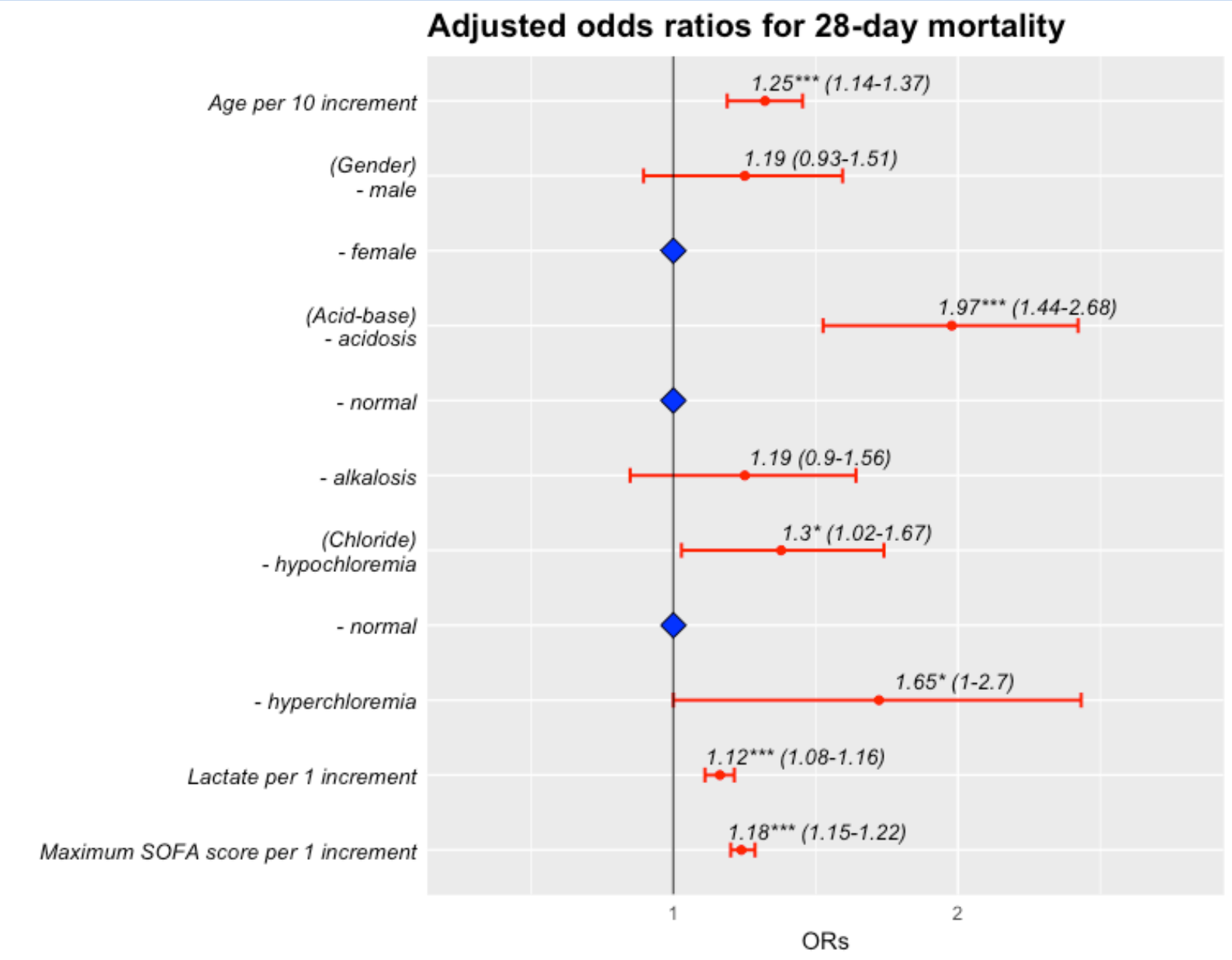


Table 1. Subgroup analysis based on acid-base state.

| Variable       | Subgroup  | OR   | Lower CI | Upper CI | P-value |
|----------------|-----------|------|----------|----------|---------|
| hypochloremia  | acidosis  | 1.84 | 1.13     | 3.01     | 0.014   |
|                | normal pH | 1.23 | 0.8      | 1.88     | 0.351   |
|                | alkalosis | 1.13 | 0.76     | 1.67     | 0.550   |
| hyperchloremia | acidosis  | 1.08 | 0.49     | 2.39     | 0.855   |
|                | normal pH | 2.14 | 1.01     | 4.57     | 0.048   |
|                | alkalosis | 2.26 | 0.79     | 6.43     | 0.126   |

Table 2. Baseline characteristics, clinical and outcome variables.

| Variable                                               | hypochloremia(< 98 mEq/L)<br>(37.3%, n=760) | normal(98-110 mEq/L)<br>(58.01%, n=1182) | hyperchloremia(>110 mEq/L)<br>(4.6%, n=95) | Total (n=2037)  | p-value |
|--------------------------------------------------------|---------------------------------------------|------------------------------------------|--------------------------------------------|-----------------|---------|
| Age, year                                              | 65.9 ± 13.3                                 | 68.7 ± 13.3                              | 72.0 ± 12.8                                | 67.8 ± 13.4     | 0.000   |
| Male, %                                                | 453 (59.61%)                                | 705 (59.64%)                             | 48 (50.53%)                                | 1206 (59.20%)   | 0.211   |
| Systolic blood pressure, mmHg                          | 97.71 ± 28.04                               | 100.34 ± 30.53                           | 96.03 ± 29.31                              | 99.16 ± 29.59   | 0.092   |
| Diastolic blood pressure, mmHg                         | 59.56 ± 18.96                               | 60.59 ± 19.22                            | 59.23 ± 20.60                              | 60.14 ± 19.19   | 0.457   |
| Hypertension, %                                        | 296 (38.95%)                                | 507 (42.89%)                             | 41 (43.16%)                                | 844 (41.43%)    | 0.213   |
| Diabetes mellitus, %                                   | 250 (32.89%)                                | 342 (28.93%)                             | 34 (35.79%)                                | 626 (30.73%)    | 0.100   |
| Cardiovascular disease, %                              | 100 (13.16%)                                | 162 (13.71%)                             | 11 (11.58%)                                | 273 (13.40%)    | 0.817   |
| Cerebrovascular disease, %                             | 76 (10.00%)                                 | 147 (12.44%)                             | 24 (25.26%)                                | 247 (12.13%)    | 0.000   |
| Chronic lung disease, %                                | 71 (9.34%)                                  | 91 (7.70%)                               | 2 (2.11%)                                  | 164 (8.05%)     | 0.040   |
| Hematologic malignancy, %                              | 58 (7.63%)                                  | 78 (6.60%)                               | 6 (6.32%)                                  | 142 (6.97%)     | 0.661   |
| Metastatic cancer, %                                   | 222 (29.21%)                                | 236 (19.97%)                             | 10 (10.53%)                                | 468 (22.97%)    | 0.000   |
| Chronic renal disease, %                               | 58 (7.63%)                                  | 88 (7.45%)                               | 15 (15.79%)                                | 161 (7.90%)     | 0.014   |
| Chronic liver disease, %                               | 102 (13.42%)                                | 129 (10.91%)                             | 10 (10.53%)                                | 241 (11.83%)    | 0.229   |
| Dementia, %                                            | 24 (3.16%)                                  | 87 (7.36%)                               | 12 (12.63%)                                | 123 (6.04%)     | 0.000   |
| Presence of transplanted organ, %                      | 17 (2.24%)                                  | 18 (1.52%)                               | 3 (3.16%)                                  | 38 (1.87%)      | 0.333   |
| WBC * 10^3, mm^3                                       | 14.28 ± 21.89                               | 12.55 ± 13.18                            | 11.26 ± 8.26                               | 13.13 ± 16.83   | 0.046   |
| Neutrophil, %                                          | 76.25 ± 23.39                               | 77.64 ± 21.79                            | 77.72 ± 20.94                              | 77.11 ± 22.38   | 0.417   |
| Platelet, *10^3, mm^3                                  | 168.15 ± 124.10                             | 163.23 ± 118.57                          | 161.55 ± 104.18                            | 164.99 ± 120.02 | 0.651   |
| Sodium, mmol/L                                         | 130.57 ± 5.32                               | 136.83 ± 4.14                            | 145.41 ± 6.52                              | 134.90 ± 6.06   | 0.000   |
| Potassium, mmol/L                                      | 4.31 ± 0.89                                 | 4.18 ± 0.77                              | 4.16 ± 1.12                                | 4.23 ± 0.84     | 0.003   |
| Chloride, mmol/L                                       | 92.79 ± 4.23                                | 102.46 ± 3.35                            | 114.99 ± 4.06                              | 99.43 ± 6.86    | 0.000   |
| Blood urea nitrogen, mg/dL                             | 33.91 ± 21.96                               | 31.07 ± 19.18                            | 48.29 ± 32.94                              | 32.94 ± 21.38   | 0.000   |
| Creatinine, mg/dL                                      | 1.96 ± 1.67                                 | 1.68 ± 1.21                              | 2.22 ± 2.21                                | 1.81 ± 1.46     | 0.000   |
| Albumin, g/dL                                          | 2.93 ± 0.67                                 | 2.99 ± 0.66                              | 2.62 ± 0.65                                | 2.95 ± 0.67     | 0.000   |
| hs-CRP, mg/dL                                          | 16.47 ± 12.42                               | 13.57 ± 12.48                            | 13.76 ± 10.83                              | 14.66 ± 12.46   | 0.000   |
| Procalcitonin, ng/mL                                   | 27.21 ± 58.07                               | 29.10 ± 64.97                            | 22.00 ± 34.98                              | 28.09 ± 61.42   | 0.584   |
| pH                                                     | 7.42 ± 0.12                                 | 7.41 ± 0.10                              | 7.36 ± 0.13                                | 7.41 ± 0.11     | 0.000   |
| PCO2, mmHg                                             | 29.77 ± 12.12                               | 29.36 ± 9.66                             | 29.93 ± 11.54                              | 29.54 ± 10.73   | 0.667   |
| PO2, mmHg                                              | 85.80 ± 40.93                               | 85.14 ± 41.34                            | 94.46 ± 57.52                              | 85.82 ± 42.10   | 0.116   |
| Bicarbonate, mEq/L                                     | 19.59 ± 6.00                                | 18.81 ± 4.90                             | 16.96 ± 6.49                               | 19.02 ± 5.44    | 0.000   |
| SaO2, %                                                | 93.08 ± 9.32                                | 92.98 ± 9.03                             | 91.72 ± 10.06                              | 92.96 ± 9.19    | 0.393   |
| Lactate, mmol/L                                        | 4.59 ± 3.71                                 | 4.04 ± 3.00                              | 3.96 ± 2.68                                | 4.24 ± 3.28     | 0.001   |
| Sequential organ failure assessment(SOFA)              | 8.51 ± 3.83                                 | 8.31 ± 3.80                              | 10.05 ± 3.60                               | 8.46 ± 3.81     | 0.000   |
| Acute physiology and chronic health evaluation(APACHE) | 21.09 ± 8.96                                | 19.81 ± 9.10                             | 23.87 ± 10.01                              | 20.48 ± 9.14    | 0.000   |
| 28-day death, %                                        | 181 (23.82%)                                | 227 (19.20%)                             | 33 (34.74%)                                | 441 (21.65%)    | 0.000   |