

# Hyponatraemia in elderly emergency department patients: A marker of frailty

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## ABSTRACT

Background: Details on hyponatraemia in the emergency department are limited, especially regarding older patients, a population more susceptible to hyponatraemia and its effects. Our objective was to gain insight into the prevalence, aetiology, treatment and prognosis of clinically relevant hyponatraemia in elderly emergency department patients. The impact of the severity of hyponatraemia on outcome was a secondary objective.

Methods: A retrospective cohort study of 1438 internal medicine patients aged  $\geq 65$  years presenting to the emergency department between 1 September 2010 and 31 August 2011 was performed. Clinically relevant hyponatraemia was defined as a serum sodium level  $< 130$  mmol/l. The reference group had a serum sodium level of 130-145 mmol/l. Hyponatraemia was subdivided into moderate (129-125 mmol/l), and severe ( $< 125$  mmol/l). Results: Ninety-one elderly patients (6.3%) were hyponatraemic at presentation to the emergency department. The main causes were the use of diuretics, hypovolaemia, and the syndrome of inappropriate antidiuretic hormone secretion (57.1%). Hyponatraemia was associated with higher admission rates (93.4 vs. 72.9%) and longer hospital stay (8 vs. 6 days) vs. the reference group. Three-month survival rate in hyponatraemic elderly patients was 74% (95% CI 64-84%) vs. 83% (95% CI 81-85%) in the reference group. Moderate hyponatraemia was associated with an increased risk of death (HR 1.7, 95% CI 1.2-2.4) vs. the reference group after multivariable adjustment for age and comorbidity.

Conclusion: Hyponatraemia, a common electrolyte disturbance among elderly internal medicine patients presenting to the emergency department, was associated with higher admission rates, longer hospital stay, and higher mortality rates. In particular, moderate hyponatraemia was a marker of underlying frailty and predictive of mortality.

## KEYWORDS

Emergency department, frail elderly, hyponatraemia, outcome

## INTRODUCTION

Hyponatraemia is the most common electrolyte disturbance encountered in clinical practice.<sup>1</sup> The prevalence of hyponatraemia varies widely depending on the clinical setting. The highest frequencies are observed in intensive care unit (ICU) patients, in the postoperative setting, and in older patients admitted to geriatric wards.<sup>2,3</sup> The elderly are particularly susceptible to developing hyponatraemia, due to age-related physiological changes in water and electrolyte balance, the presence of comorbid conditions, and polypharmacy.<sup>4-6</sup>

Diagnostic evaluation of hyponatraemia can be challenging, especially in elderly patients with multi-morbidity, and requires a systematic approach, including assessment of the extracellular volume status and distinction between acute and chronic hyponatraemia.<sup>7-9</sup> Although mild stable hyponatraemia is often considered to be of little clinical significance, recent studies have identified an association between hyponatraemia and complications, such as falls due to gait instability, attention deficits, and an increased risk of fractures due to osteoporosis.<sup>1,10,11</sup> These complications may be of special significance to frail older patients with hyponatraemia. Furthermore, severe hyponatraemia is a marker of serious disease and an indicator of poor prognosis.<sup>12-15</sup> Nonetheless, it remains unclear whether the higher mortality rates encountered in severe hyponatraemia are directly related to deviations in sodium levels or to underlying conditions.<sup>14,16</sup>

Information on the frequency of hyponatraemia and its impact on outcome in elderly patients in an emergency department setting is limited. Yet, this information is essential in implementing a strategy to prevent adverse health outcome in this vulnerable population. The primary goal of our study was to gain insight into the prevalence, aetiology, clinical presentation, and treatment of clinically relevant hyponatraemia in elderly medical patients presenting to the emergency department. Differences in the presentation and outcome of elderly patients with hyponatraemia versus elderly patients with normal serum sodium levels and the impact of the severity of hyponatraemia on patient outcome were secondary objectives.

## MATERIALS AND METHODS

### Study design, setting and selection of participants

A retrospective cohort study was conducted at a 500-bed teaching hospital in the Netherlands. The majority of emergency department patients are referred by a general practitioner. Other modes of presentation are referral by a medical specialist, ambulance arrival in high emergency patients, and self-referral. Patients presenting to the emergency department are assessed by an intern, a non-trainee resident, or a trainee resident supervised by a medical specialist or emergency physician.

Data on all visits of patients aged 65 years or older referred to the emergency department for internal medicine between 1 September 2010 and 31 August 2011 were extracted by two abstractors with a medical background. The abstractors were not blinded to the study hypothesis. Patients were excluded if internal medicine was not the principle treating speciality in the emergency department. The presence of hyponatraemia was identified by laboratory investigation in the emergency department. After identification of elderly patients with hyponatraemia in the emergency department, only data on the index visit were extracted. Follow-up lasted from the date of the emergency department visit until the end of at least one year of follow-up, the date of death, or the date of last available information. Institutional Review Board exemption of approval was acquired.

### Covariates

Information on baseline characteristics, medical history, and medication use as assessed in the emergency department, the date and time of the visit, clinical characteristics at presentation to the emergency department, laboratory investigation performed in the emergency department, diagnosis and hospital discharge diagnosis, serum sodium levels during admission, discharge date, and the date of last follow-up or the date

of death were retrieved from patient records. The index visit was defined as the first emergency department visit of each patient between 1 September 2010 and 31 August 2011. Triage at presentation was performed using the five-level Manchester Triage System (MTS).<sup>17,18</sup> Medical history and comorbidity as recorded in patients' emergency department records were classified according to the International Classification of Disease-10 (ICD-10) and according to the Charlson Comorbidity Index (CCI), which consists of the following categories: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular accidents, pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, severe liver disease, diabetes mellitus (with and without complications), hemiplegia or paraplegia, cancer, metastatic cancer, and human immunodeficiency virus (HIV).<sup>19</sup> Polypharmacy was defined as the use of five or more different medications.<sup>20</sup>

### Outcomes

The focus of the study was clinically relevant hyponatraemia, defined as a serum sodium level < 130 mmol/l. Moderate and severe hyponatraemia were defined as serum sodium levels between 125-129, and < 125 mmol/l, respectively. Elderly patients with a serum sodium level between 130-145 mmol/l were assigned to the reference group. Normonatraemia was defined as a serum sodium level between 135-145 mmol/l. Hypernatraemia was defined as a serum sodium level > 145 mmol/l.<sup>8</sup>

The objective of the study was to estimate the prevalence, aetiology, treatment, and correction rate of clinically relevant hyponatraemia, hospital admission, the length of hospital stay, in-hospital mortality rate, and three-month and one-year survival. In a secondary analysis, we compared hyponatraemic patients with the reference group. Data on vital status to at least one-year follow-up were obtained from patient records or by contacting their general practitioners. If the date of death was unknown, the date in between the date of the last follow-up and the date of contact with the general practitioner was selected.

### Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 19.0. Armonk, New York. Comparisons of baseline patient characteristics between hyponatraemic patients and the reference group and between the hyponatraemic severity groups were made using the Chi-square for categorical variables. Numerical variables were tested using one-way analysis of variance, the Kruskal-Wallis test, Mann-Whitney U test, and unpaired T-test, depending on the number of groups compared and the distribution pattern of the variable. Missing data were categorised as 'unknown' and included in the analyses. The prevalence of hyponatraemia was

calculated by dividing the number of hyponatraemic elderly patients by the total number of elderly patients included in the study; 95% confidence intervals (95% CI) of the prevalence were estimated assuming a normal distribution.<sup>21</sup> Overall survival was estimated using the Kaplan-Meier survival analysis. The log-rank test was used to compare survival curves. Univariable and multivariable Cox regression analyses were performed in order to estimate the effect of covariates on patient outcome, expressed as hazard ratio (HR) and 95% CI. Multivariable analysis included all variables associated with the outcome in the univariable analysis at a p-value of 0.1 and changing the point estimate by > 10% in bivariable analysis, or variables considered as clinically relevant. Effect modulation was investigated. A p-value < 0.05 was considered significant. A sensitivity analysis was performed to evaluate the effect of missing sodium values on patient survival by including patients with missing values in the reference group in the analysis.

## RESULTS

### Characteristics of study subjects

During the study period, 1438 index visits of patients aged 65 years and older presenting to the emergency department for internal medicine were identified. The reference group consisted of 1218 elderly patients. Ninety-one elderly patients were hyponatraemic (mean age 78.4 years), representing a prevalence of 6.3% (95% CI 5.2-7.7%). Serum sodium level was unknown in 84 elderly patients and 45 elderly patients were hypernatraemic. In 91 hyponatraemic patients, 58 (63.7%) were classified as moderate, and 33 (36.3%) as severe hyponatraemia. In seven patients (7.7%), the main reason for the emergency department visit was hyponatraemia. Malaise was the most prevalent symptom, namely in 15 patients (16.5%). Other reasons for the visit in hyponatraemic elderly patients included confusion or delirium in seven patients (7.7%), hyperglycaemia in three patients (3.3%),

**Table 1.** Baseline characteristics of elderly patients presenting at the emergency department

	Total (n = 1309)	Hyponatraemia (n = 91)	Reference group (n = 1218)	P-value
Mean age in years (SD) Range	77.8 (7.7) 65-99	78.4 (7.5) 65-94	77.7 (7.8) 65-99	0.447
Male patients (%)	589 (45.0%)	24 (26.4%)	565 (46.4%)	< 0.001
Medical history (%)				
No history	11 (0.8%)	1 (1.1%)	10 (0.8%)	0.860
Unknown	3 (0.3%)	-	3 (0.3%)	
Diabetes mellitus	308 (23.5%)	31 (34.1%)	277 (22.7%)	0.040
Dementia	76 (5.8%)	2 (2.2%)	74 (6.1%)	0.235
Heart failure	121 (9.2%)	11 (12.1%)	110 (9.0%)	0.488
Malignancy	358 (27.3%)	29 (31.9%)	329 (27.0%)	0.480
Respiratory condition	192 (14.7%)	10 (11.0%)	182 (14.9%)	0.443
Mean CCI (SD)	2.2 (2.1)	2.5 (2.3)	2.2 (2.1)	0.335
Medication use (%)				
Polypharmacy	766 (58.5%)	59 (64.8%)	707 (58.0%)	0.448
Unknown	119 (9.1%)	7 (7.7%)	112 (9.2%)	
Diuretics	489 (37.4%)	50 (55.6%)	439 (36.1%)	0.001
Antipsychotics	42 (3.2%)	3 (3.3%)	39 (3.2%)	0.719
Antidepressants	102 (7.8%)	6 (6.6%)	96 (7.9%)	0.616
Mean number (SD)	6.3 (3.8)	6.7 (3.8)	6.3 (3.8)	0.270
Referral (%)				
General practitioner	955 (73.0%)	73 (80.2%)	882 (72.4%)	0.189
Medical specialist	87 (6.6%)	7 (7.7%)	80 (6.6%)	
Ambulance	131 (10.0%)	7 (7.7%)	124 (10.9%)	
Self-referral	136 (10.4%)	4 (4.4%)	132 (10.8%)	
Triage by MTS (%)				
Red	16 (1.2%)	1 (1.1%)	15 (1.2%)	0.700
Orange	133 (10.2%)	11 (12.1%)	122 (10.0%)	
Yellow	744 (56.8%)	56 (61.5%)	688 (56.5%)	
Green	413 (31.6%)	23 (25.3%)	390 (32.0%)	
Blue	-	-	-	
No triage	3 (0.2%)	-	3 (0.3%)	

SD = standard deviation; CCI = Charlson Comorbidity Index; MTS = Manchester Triage System: red = immediate resuscitation, orange = very urgent, yellow = urgent, green = standard, blue = non-urgent.  
P-value for comparison of elderly patients with hyponatraemia and the reference group. P-values were estimated using the unpaired T-test, Mann-Whitney U test, and Chi-square test.

collapse or fall in four patients (4.4%), and somnolence in two patients (2.2%). Most patients presented with symptoms unrelated to hyponatraemia.

Twenty-four hyponatraemic patients (26.4%) were male compared with 565 (46.4%) in the reference group ( $p < 0.001$ ) (table 1). The comorbidity index was comparable among hyponatraemic elderly patients and the reference group (mean CCI 2.5 vs. 2.2, respectively,  $p = 0.335$ ). Diuretic use was more frequent in hyponatraemic patients than in the reference group (55.6 vs. 36.1%, respectively,  $p < 0.001$ ). Hyponatraemic elderly patients were more often diabetic compared with the reference group (table 1). Hyponatraemic elderly patients had a higher C-reactive protein level (44.5 vs. 23 mg/l, respectively,  $p = 0.022$ ) than the reference group. Primary diagnoses made in the emergency department were similar in hyponatraemic elderly patients and the reference group. Fifty-three elderly patients (3.7%) were lost to follow-up, of which 47 (3.9%) patients were in the reference group, one (1.1%) was hyponatraemic, two (4.4%) were hypernatraemic, and for three (3.6%) patients, sodium level was unknown.

Elderly patients with unknown serum sodium levels ( $n = 84$ ) were younger (75.9 vs. 77.7 years, respectively,  $p = 0.035$ ) than elderly patients in the reference group. They had lower comorbidity levels (mean CCI 1.5 vs. 2.2, respectively,  $p = 0.005$ ) and were less frequently admitted to the hospital (29.8 vs. 72.9%, respectively,  $p < 0.001$ ). The most common presenting symptom was (suspected) deep venous thrombosis ( $n = 23$ , 27.4%), as opposed to malaise in patients for whom sodium data were available.

#### Aetiology and treatment

A minority of patients received an advanced diagnostic work-up in the emergency department to determine the cause of hyponatraemia, such as measurement of blood osmolality (22.0%), urine osmolality (23.1%), and urine sodium (45.1%). The presumed cause of the hyponatraemia

was specified in the emergency department charts of 62 patients (68.1%). The use of diuretics was considered the primary cause ( $n = 25$ , 27.5%), followed by hypovolaemia ( $n = 14$ , 15.4%) and syndrome of inappropriate antidiuretic hormone secretion (SIADH) ( $n = 13$ , 14.3%). Other causes were hyperglycaemia ( $n = 2$ , 2.2%), renal insufficiency ( $n = 2$ , 2.2%), and heart failure ( $n = 3$ , 3.3%).

In 83.5% of the hyponatraemic elderly patients ( $n = 76$ ), therapy to correct the serum sodium was started in the emergency department. The most frequently used method of correction ( $n = 28$ , 30.8%) was a combination of the infusion of isotonic sodium chloride (0.9% NaCl) and cessation of medication; 26.4% of elderly patients ( $n = 24$ ) received 0.9% NaCl infusion. Other methods of correction were cessation of medication ( $n = 6$ , 6.6%), fluid restriction ( $n = 7$ , 7.7%), hypertonic sodium chloride infusion (3% NaCl) ( $n = 4$ , 4.4%), or other combination therapy ( $n = 7$ , 7.7%). Treatment time in the emergency department was similar for hyponatraemic patients and the reference group (median 161 vs. 162 minutes, respectively,  $p = 0.450$ ) and hyponatraemic patients with and without a cause specified (162 vs. 159 minutes, respectively,  $p = 0.655$ ).

The median initial rate of sodium correction in the severe hyponatraemia group ( $n = 32$ ) was 0.53 mmol/l/hour (range 0.06–2.8 mmol/l/hour) during the first ten hours of correction. In nine patients with severe hyponatraemia (27.3%), the rate of correction exceeded 10 mmol/l/24 hours. No patients developed osmotic demyelination syndrome. Six (6.6%) elderly patients were discharged home from the emergency department with hyponatraemia. Eleven hyponatraemic patients (15.3%) still had a serum sodium level  $< 130$  mmol/l at time of hospital discharge.

#### Patient outcome

Hyponatraemia in elderly emergency department patients was associated with higher admission levels (93.4 vs. 72.9%, respectively,  $p < 0.001$ ) and longer median hospital

**Table 2.** Outcome in hyponatraemic elderly patients vs. the reference group

	Total (n = 1309)	Hyponatraemia (n = 91)	Reference group (n = 1218)	P-value
Hospital admission (%)	973 (74.3%)	85 (93.4%)	888 (72.9%)	$< 0.001$
Median length of hospital stay in days (range)	6 (1–91)	8 (1–64)	6 (1–91)	0.021
ICU/MCU admission (%)	32 (3.3%)	2 (2.4%)	30 (3.4%)	0.051
Death during admission (%)	96 (9.9%)	13 (15.3%)	83 (9.3%)	0.087
ED return visits $< 3$ months (%)	316 (24.1%)	14 (15.4%)	302 (24.8%)	0.085
Three-month survival (95% CI)	82% (80–84%)	74% (64–84%)	83% (81–85%)	
One-year survival (95% CI)	68% (66–70%)	53% (43–63%)	69% (67–71%)	

ICU = Intensive Care Unit, MCU = Medium Care Unit, SD = standard deviation, 95%CI = 95% confidence interval. P-values for comparison of outcome in elderly patients with hyponatraemia and the reference group. P-values were estimated using the Mann-Whitney U test and Chi-square test. One-year survival was calculated with Kaplan-Meier analysis.

stay (8 vs. 6 days, respectively,  $p = 0.021$ ) compared with the reference group (table 2). Hospitalised elderly patients with hyponatraemia ( $n = 85$ ) had higher triage levels compared with hyponatraemic patients who were discharged home from the emergency department ( $n = 6$ ). Comorbidity levels and medication use were comparable among hospitalised and discharged hyponatraemic elderly patients. The three-month survival rate of hyponatraemic elderly patients directly discharged from the emergency department was 100 vs. 72% (95% CI 62-82%) in hospitalised hyponatraemic elderly patients. The in-hospital mortality rate of elderly patients with hyponatraemia was 15.3% ( $n = 13$ ), in contrast to 9.3% ( $n = 83$ ) in older patients from the reference group ( $p = 0.087$ ). Three-month and one-year survival in all hyponatraemic elderly patients were 74% (95% CI 64-84%) and 53% (95% CI 43-63%) vs. 83% (95% CI 81-85%) and 69% (95% CI 67-71%) respectively in the reference group. Complete ( $n = 61$ ) or incomplete ( $n = 11$ ) correction of the sodium level during hospitalisation did not influence one-year survival (57%, 95% CI 45-69% vs. 73%, 95% CI 48-98%, respectively). After multivariable adjustment for age and CCI, and a combination of age, CCI and C-reactive protein, hyponatraemia was independently associated with higher mortality rates among elderly patients (HR 1.5, 95% CI 1.1-2.1 and HR 1.5, 95% CI 1.1-2.0) compared with the reference group (table 3). Sensitivity analysis, performed to evaluate the effect of missing sodium values on patient outcome, revealed no change in one-year survival (70%, 95% CI 68-72%), when considering all patients with unknown sodium values as part of the reference group.

**Table 3.** Unadjusted and adjusted hazard ratio and 95% confidence intervals for mortality in hyponatraemic elderly patients compared with the reference group.

	Total (n = 91)	Moderate (n = 58)	Severe (n = 33)
Crude HR	1.5 (1.1-2.0)	1.7 (1.2-2.4)	1.2 (0.7-2.1)
Age-adjusted	1.5 (1.1-2.0)	1.6 (1.1-2.2)	1.2 (0.7-2.1)
CCI-adjusted	1.6 (1.2-2.2)	1.8 (1.2-2.5)	1.3 (0.8-2.2)
Malignancy-adjusted	1.5 (1.1-2.1)	1.6 (1.1-2.3)	1.4 (0.8-2.4)
CRP-adjusted	1.4 (1.0-1.9)	1.5 (1.1-2.2)	1.1 (0.7-2.0)
Multivariable adjusted 1	1.5 (1.1-2.1)	1.7 (1.2-2.4)	1.3 (0.8-2.3)
Multivariable adjusted 2	1.5 (1.1-2.0)	1.5 (1.1-2.2)	1.3 (0.7-2.2)

1 Adjusted for age and CCI, 2 Adjusted for age, CCI, and CRP levels. HR = hazard ratio, 95%CI = 95% confidence interval, CCI = Charlson Comorbidity Index, CRP = C-reactive protein. Variables initially considered as potential confounders: referral pattern, gender, history of diabetes, respiratory condition and heart failure, total number of medications, polypharmacy, and diuretics.

### Subgroup analysis of hyponatraemia categories

CCI and diuretic use were comparable among patients with moderate and severe hyponatraemia (table 4). Severely hyponatraemic patients presented more often to the emergency department with symptoms related to hyponatraemia (36.4%) compared with moderately hyponatraemic patients (22.4%). Diagnostic work-up was increasingly complete with worsening of serum sodium (table 4). The C-reactive protein level was 78.5 mg/l in moderate, and 12 mg/l in severe hyponatraemia. In 29 (87.9%) of the severely hyponatraemic patients, the aetiology of the sodium disorder was registered in

**Table 4.** Characteristics of elderly patients, subdivided into moderate, and severe hyponatraemia

	Moderate (n = 58)	Severe (n = 33)	P-value
Mean age in years (SD)	78.8 (7.8)	77.6 (7.0)	0.191
Male patients	15 (25.9%)	9 (27.3%)	1.000
Medical history (%)			
Heart failure	8 (13.8%)	3 (9.1%)	0.740
Dementia	1 (1.7%)	1 (3.0%)	1.000
Diabetes mellitus	18 (31.0%)	13 (39.4%)	0.492
Malignancy	22 (37.9%)	7 (21.2%)	0.109
Respiratory condition	4 (6.9%)	6 (18.2%)	0.160
Mean CCI (SD)	2.5 (2.1)	2.3 (2.5)	0.640
Medication use (%)			
Polypharmacy	37 (63.8%)	22 (66.7%)	0.837
Unknown	4 (6.9%)	3 (9.1%)	
Diuretics	32 (55.1%)	18 (54.5%)	0.964
Total number (SD)	6.6 (4.0)	7.0 (3.6)	0.671
Diagnostic work-up on ED (%)			
Blood osmolality	8 (13.8%)	12 (36.4%)	0.018
Urine osmolality	10 (17.2%)	11 (33.3%)	0.119
Urine sodium	19 (32.8%)	22 (66.7%)	0.002
Cause of hyponatraemia (%)			0.002
No cause specified	25 (43.1%)	4 (12.1%)	
Diuretics	13 (22.4%)	12 (36.4%)	
Hypovolaemia	10 (17.2%)	4 (12.1%)	
SIADH	3 (5.2%)	10 (30.3%)	
Hyperglycaemia	1 (1.7%)	1 (3.0%)	
Renal insufficiency	2 (3.4%)	-	
Heart failure	2 (3.4%)	1 (3.0%)	
Other	2 (3.4%)	1 (3.0%)	
Admission (%)	53 (91.4%)	32 (97.0%)	0.411
Median hospital LOS in days (range)	9 (1-64)	7 (1-29)	0.492
Death during admission (%)	10 (18.9%)	3 (9.4%)	0.290
Three-month survival (95%CI)	74% (62-86%)	73% (57-89%)	

SD = standard deviation, ED = emergency department, CCI = Charlson Comorbidity Index, SIADH = syndrome of inappropriate antidiuretic hormone secretion, LOS = length of stay, CI = confidence interval. P-value for trend in comparison of moderate, and severe hyponatraemia. P-values were estimated using the unpaired T-test, Mann-Whitney U test, and Chi-square test



the emergency department, compared with 33 (56.9%) in moderate hyponatraemia ( $p < 0.002$ ). The primary cause of severe hyponatraemia was the use of diuretics ( $n = 12$ , 36.4%), followed by SIADH ( $n = 10$ , 30.3%) and hypovolaemia ( $n = 4$ , 12.1%). Treatment was started in the emergency department in 32 (97.0%) of the patients with severe hyponatraemia, and 44 (75.9%) of the patients with moderate hyponatraemia ( $p = 0.015$ ). Admission rates were similar in both hyponatraemia categories (table 4). One-year survival was 50% (95% CI 36-64%), and 58% (95% CI 40-76%) for moderate, and severe hyponatraemia, respectively. Adjustment for age, CCI and a combination of age, CCI, and C-reactive protein levels revealed an increased risk of death in patients with moderate hyponatraemia (HR 1.7, 95% CI 1.2-2.4 and HR 1.5, 95% CI 1.1-2.2, respectively) vs. elderly patients in the reference population (figure 1) (table 3).

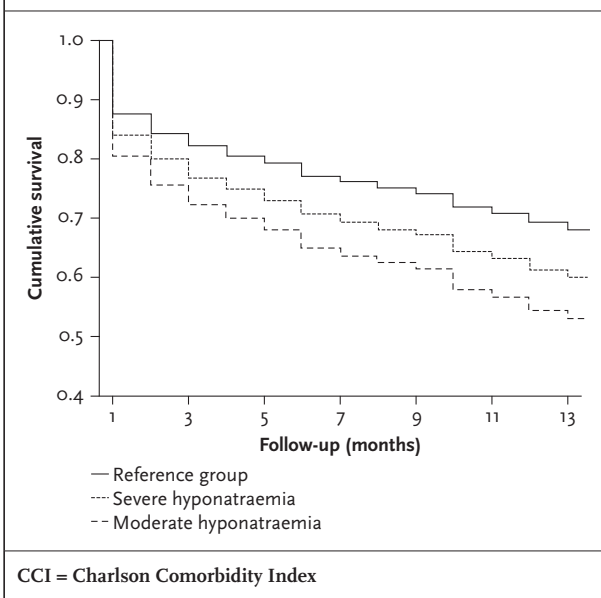
## DISCUSSION

In this retrospective cohort study, we report a prevalence of clinically relevant hyponatraemia (serum sodium level  $< 130$  mmol/l) of 6.3% in elderly internal medicine patients presenting to the emergency department. Research in hospitalised patients, focusing solely on elderly patients, reported a prevalence of 16.7-34.5%,<sup>13,16,22,23</sup> which is considerably higher than our results. However, comparison of our results remains difficult, since the cut-off value for hyponatraemia as well as the clinical setting vary among studies resulting in different prevalence rates.<sup>7,24-27</sup>

Few elderly patients presented to the emergency department solely for analysis of hyponatraemia. This corresponds with findings that hyponatraemia was not an isolated disease, but rather an additional factor to an underlying disorder.<sup>13</sup> Remarkably, only a minority of patients received an appropriate diagnostic work-up according to the emergency department guideline.<sup>28</sup> In addition, the cause of hyponatraemia was specified in only 68.1% of hyponatraemic patients in the emergency department. Although both observations apply particularly to cases with moderate hyponatraemia, incomplete or lack of analysis could possibly lead to inadequate treatment in this group and consequently adverse patient outcome. However, due to the retrospective nature of the study, some of the clinical assessment steps in the emergency department were perhaps not accurately documented, but were in fact part of diagnostic work-up and treatment. In addition, we found an adequate median correction rate of 0.53 mmol/l/hour during the first ten hours of correction in severely hyponatraemic patients, the subgroup with the highest risk of complications.<sup>28</sup> Furthermore, even though the advised correction rate of 10 mmol/l/24 hours was exceeded in nine patients with severe hyponatraemia, no cases of osmotic demyelination syndrome occurred. Blood osmolality, however, was known in only 22.0% of hyponatraemic elderly, and therefore it was not possible to accurately identify pseudohyponatraemia or hyperosmolar hyponatraemia. Still, our analysis of all sodium values showed that hyponatraemia regardless of underlying pathophysiology is an adverse prognosticator in elderly emergency department patients.

Our study confirms previous findings that hyponatraemia is an indicator of poor prognosis, such as longer hospital stay and higher mortality rates.<sup>14,24,26</sup> In particular, patients with moderate hyponatraemia had the highest mortality rate compared with the reference group, even after adjustment for age, CCI, and C-reactive protein levels. We found no relationship between mortality in moderate hyponatraemia and the presence of an acute critical illness at emergency department presentation as is reflected by comparable triage levels among hyponatraemia groups. The increased mortality risk in elderly patients with moderate hyponatraemia may be due to a lack of guideline adherence, leading to underdiagnosing and undertreating of elderly patients with moderate hyponatraemia.<sup>29</sup> In addition, moderate hyponatraemia was frequently an additional finding in other underlying disorders. The therapy indicated for these disorders may not be appropriate for hyponatraemia. Moreover, the failure of physicians to identify the increased health risk associated with asymptomatic hyponatraemia in this frail population may contribute to adverse patient outcome. Since hyponatraemia, especially moderate hyponatraemia, is probably a good marker of frailty and a poor prognosis in older patients as is consistent with previous

**Figure 1.** Survival in patients with moderate, and severe hyponatraemia and the reference group after adjustment for age and CCI



research,<sup>23</sup> it emphasises the need to adequately assess and treat hyponatraemia in elderly patients, in addition to careful monitoring of their general condition.

Our findings may have been influenced by several limitations. Firstly, due to the single-centre setting, our findings may not be generalisable to other populations. Secondly, there is a potential for bias, because of the retrospective observational design and as a result of incomplete data. Furthermore, the inability to determine the specific reason for measuring sodium levels in this retrospective cohort is a potential source of bias. Additionally, because of the availability of nursing home physicians in the Netherlands, elderly nursing home residents may have been underrepresented, since these patients are less likely to be sent to the emergency department for evaluation. Therefore, the results of our study may not be applicable to this patient group. Moreover, despite our efforts to correct for confounders detected in previous research or encountered in this study, residual bias may remain. Lastly, the relatively small number of patients with severe hyponatraemia may contribute to reduced reliability of our results.

Future prospective research should focus on the impact of hyponatraemia on patient outcome specifically relevant to the elderly, such as the risk of cognitive and functional decline. In addition, whether improvement in the care of elderly hyponatraemic patients on the emergency department can result in a reduction of adverse outcome remains an important research question.

In summary, hyponatraemia is common among elderly internal medicine patients visiting the emergency department and is associated with adverse outcome. Moderate hyponatraemia seems to be of special importance to the elderly, as it appears to be a marker for frailty and predictive of mortality in this population. Improvement in adequately diagnosing and treating hyponatraemia in elderly emergency department patients is important, yet more attention to the general condition of this frail population is essential.

## Disclosure

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