

# Copeptin for the differential diagnosis and therapy management of hyponatremia in hospitalized patients "The Co-MED-Study"

Nicole Nigro, Bettina Winzeler, Isabelle Suter, Birsen Arici, Martina Bally, Claudine Blum, Philipp Schuetz, Christian Nickel, Roland Bingisser, Andreas Bock, Andreas Huber, Beat Müller, Mirjam Christ-Crain

## Background & Aim

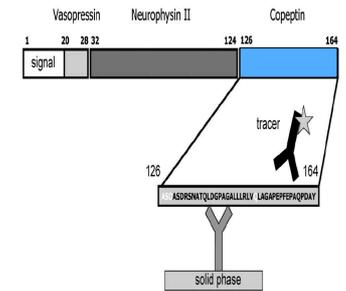
### Background:

- Hyponatremia is the most common electrolyte disorder in clinical routine and its differential diagnosis is challenging
- The most important osmo- and volume-regulated hormone is arginine vasopressin (AVP). The amount of plasma AVP is regulated by osmotic and non-osmotic stimuli
- The measurement of AVP is cumbersome
- Copeptin is more stable, released in an equimolar ratio with AVP and can be assayed in plasma

### Aim of the study:

- To evaluate the usefulness of copeptin as a new diagnostic and prognostic tool in the differential diagnosis and in therapy management of profound hyponatremia

Figure 1: Copeptin, the C-terminal Glycopeptide of the AVP Precursor pre-provasopressin



## Patients & Methods

### Setting:

- All patients admitted to the University Hospital of Basel and the Kantonsspital Aarau with profound hyponatremia ( $\text{Na}^+ < 125 \text{ mmol/L}$ ) were included in the study

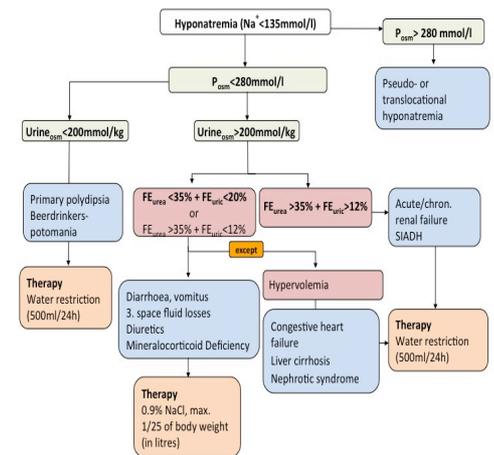
### Work-up on admission:

- Complete medical history
- Clinical items (physical examination, volume status, HR, BP, temp., weight, etc.)
- Routine laboratory tests and copeptin measurements

### Final diagnosis:

- The final diagnosis was made retrospectively by three experts blinded to copeptin levels and was based on our clinical algorithm (see Figure 2), complete chart review and therapy response

Figure 2: Clinical Algorithm

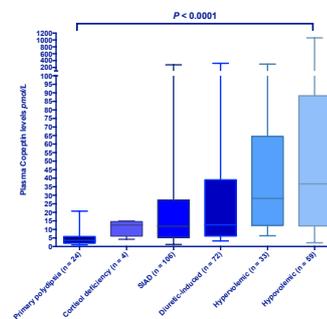


## Results

Table 1: Baseline Characteristics at Admission Overall and by Treatment Group

Characteristics	All patients (N= 298)	Fluid restriction (n= 159)	Saline infusion (n= 139)	P
% of study cohort	100.0%	53.4%	46.6%	0.120
Median [IQR] age, y	71 [60-81]	67 [56-77]	76 [66-83]	<0.001
Female, % (n)	65.4% (195)	64.2% (102)	66.9% (93)	0.63
Admission due to hyponatremia	43.6% (136)	40.3% (84)	51.8% (72)	0.043
Median [IQR] laboratory variables				
Serum sodium, mmol/L	120 [116-123]	120 [116-122]	120 [116-123]	0.83
Serum copeptin, pmol/L	14.44 [5.69-39.31]	12.16 [4.99-28.15]	21.40 [10.00-63.03]	<0.001
Copeptin/urine sodium ratio	0.33 [0.11-1.01]	0.27 [0.09-0.81]	0.39 [0.14-1.36]	0.003
FE <sub>urea</sub> , %	36.80 [29.60-46.90]	41.72 [31.93-52.81]	33.35 [28.58-42.80]	<0.001
FE <sub>UA</sub> , %	10.60 [7.39-15.10]	12.97 [9.21-18.04]	9.3 [6.11-11.70]	<0.001
Urine sodium, mmol/L	51 [29-90]	54 [27-90]	50 [30-70]	0.159
Urine osmolality, mmol/L	371 [277-494]	373 [269-464]	371 [295-485]	0.56
Median [IQR] vital signs				
Systolic blood pressure, mmHg	136 [118-154]	138 [120-156]	133 [114-152]	0.123
Diastolic blood pressure, mmHg	71 [62-81]	74 [64-84]	68 [59-79]	0.005
Heart beats/min	79 [69-90]	79 [69-90]	80 [67-90]	0.56
Temperature, °C	37.0 [36.5-37.5]	37.0 [36.4-37.4]	37.0 [36.6-37.7]	0.23
Vollemic status, % (n)				
Hypovolemic	27.5% (82)	13.2% (21)	43.9% (61)	<0.001
Euvolemic	58.1% (173)	64.2% (102)	51.1% (71)	0.035
Hypervolemic	14.4% (43)	22.6% (36)	5.0% (7)	<0.001
Outcomes, % (n)				
All-cause mortality	4.0% (12)	3.1% (5)	5.0% (7)	0.56
ICU stay	34.6% (103)	36.5% (58)	32.4% (45)	0.47

Figure 3: Copeptin and Differential Diagnosis of Hyponatremia



Copeptin levels  $< 4.4 \text{ pmol/L}$  ( $> 56.8 \text{ pmol/L}$ ) predicted fluid restriction (volume administration) with 86% (91%) specificity.

Figure 4: Copeptin and Treatment Response

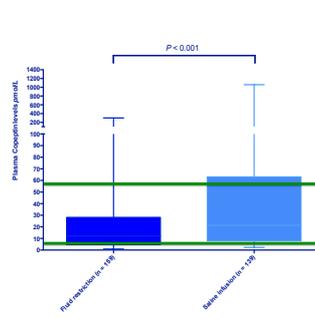
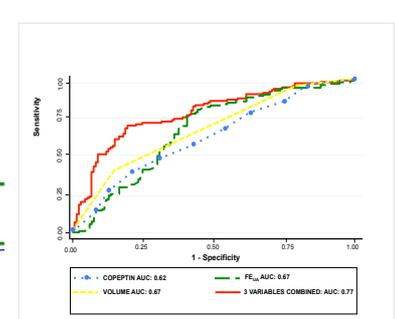


Figure 5: ROC Curves to Predict Therapy Management



Combining copeptin, vollemic status, and  $\text{FE}_{\text{UA}}$  improves the prediction for fluid therapy.

## Summary & Conclusion

Plasma copeptin levels in the differential diagnosis of profound hyponatremia show a wide overlap. Nevertheless, copeptin levels identify a subset of patients with a clear need of saline infusion or fluid restriction and may be a helpful new tool for a more rapid and targeted treatment in patients presenting with profound hyponatremia. The best prediction of therapeutic management is achieved when combining copeptin, volume status and  $\text{FE}_{\text{uric acid}}$ .