VALUE OF COPEPTIN MEASUREMENT AS A NOVEL BIOMARKER FOR PROGNOSIS INACUTE HEART FAILURE

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Introduction

Heart failure (HF) is a major cause of cardiovascular mortality and morbidity with an upward trend, Incidence rate in adults is 1-2% and the mortality rates as high as 50% for five years. There are several established markers used inHF, including neurohormones; particularly, brain natriuretic peptide (BNP) and N-terminal proBNP were shown as important markers in routine clinical practice. Copeptin (a peptide consisting of 39 amino acids) is a fragment of pre-pro-vasopressin that is synthesized and secreted in equimolar amounts to vasopressin. In contrast to AVP, copeptin is stable and can be easily measured, and an advanced assay system for C-terminal pro-AVP (copeptin) was developed over the past decade. Copeptin was shown as an independent prognostic marker of cardiovascular diseases in large, prospective clinical studies (Morgenthaler 2010, Balling and Gustafsson 2014). Plasma AVP and copeptin levels change rapidly in response to various physiological challenges. However, little is known regarding changes in plasma copeptin levels during HF treatment. Several previous studies revealed that copeptin is a strong prognostic biomarker for patients with chronic heart failure and acute decompensated heart failure.

Aim of the work

Was to evaluate the prognostic role of copeptin in acute heart failure either de novo or on top of chronic heart failure and its correlation with adverse cardiac events (death, rehospitalization and arrhythmias).

Subjects and Methods

Subjects: The present study prospectively enrolled 45 consecutive patients who had previously been referred to department of cardiology and angiology of Alexandria Main University Hospital (AMUH) with AHF between May 2019 and November 2019. exclusion criteria were: severe pulmonary disease either exacerbating bronchial asthma or chronic obstructive pulmonary disease, acute myocardial infarction, cardiogenic shock, sepsis or active infection, life threatening arrhythmias (ventricular tachycardia & complete heart block) or end stage renal disease with estimated glomerular filtration rate (eGFR) ≤ 15 ml/min.

Methods: Copeptin was measured on first day (D1) and after 72 hours (D3) of hospitalization. Copeptin was detected with a double-antibody sandwich enzyme-linked immune sorbent assay (ELISA) using Human Copeptin ELISA Kit.

Results

Table (1): Comparison between survival an non-survivalgroups according to demographic data

	Total (n = 45)	Outcome: Non-survived (n = 15)	Outcome: Survived (n = 30)	p
Sex				
Male	35(77.8%)	13(86.7%)	22(73.3%)	FEp=0.456
Female	10(22.2%)	2(13.3%)	8(26.7%)	
Age (years)				
Mean ± SD.	61.7 ± 9.8	70.7 ± 6.7	57.2 ± 7.7	<0.001*
Median (Min. – Max.)	60(45 – 83)	70(60 – 83)	57(45 – 77)	
Smoking	26 (57.8%)	13 (86.7%)	13 (43.3%)	0.006*
NYHA				
III	19 (42.2%)	0 (0%)	19 (63.3%)	<0.001*
IV	26 (57.8%)	15 (100%)	11 (36.7%)	
Heart rate (b/m)				
Mean ± SD.	81.4 ± 11	87.7 ± 13.2	78.2 ± 8.3	0.032*
Median (Min. – Max.)	80(55 – 116)	80(70 – 116)	80(55 – 90)	
Ejection fraction %				
<40	29 (64.4%)	14 (93.3%)	15 (50%)	0.004*
≥40	16 (35.6%)	1 (6.7%)	15 (50%)	
Mean ± SD.	35.6 ± 10.9	27.3 ± 10.2	39.73 ± 8.7	<0.001*
Median (Min. – Max.)	35(11 – 63)	25(11 – 55)	38(29 – 63)	
Arrhythmias				
No arrhythmias	31(68.9%)	6(40%)	25(83.3%)	MCp=0.004*
AF	9(20%)	7(46.7%)	2(6.7%)	
PVCs	5(11.1%)	2(13.3%)	3(10%)	
CrCL (ml/min)				
Mean ± SD.	46.2±14	33.8±8.3	52.4±12	<0.001*
Median (Min. – Max.)	45(22.5 – 79)	30(22.5 – 50)	55.5(30 – 79)	
Na (mg/dl)				
Mean ± SD.	139.6±2.2	139.1±2.6	139.8±2	0.351
Median (Min. – Max.)	140(135 – 145)	139(135 – 145)	140(136 – 145)	
Copeptin (pmol/L)				
Day 1				
Mean ± SD.	3 ± 1.2	3.6 ± 1.8	2.6 ± 0.5	0.008*
Median (Min. – Max.)	2.6(1.5 – 8.1)	2.7(2.4 – 8.1)	2.5(1.5 – 4.2)	
Day 3				
Mean ± SD.	3 ± 1.2	3.6 ± 1.8	2.6 ± 0.5	<0.001*
Median (Min. – Max.)	2.6(1.7 – 11.2)	3.2(2.7 – 11.2)	2.4(1.7 –3)	
Change	↑0.14±0.93	↑0.86±1.17	↓0.21±0.52	<0.001*
Medication				
Furosemide	24 (53.3%)	13 (86.7%)	11 (36.7%)	0.002*
Aspirin	22 (48.9%)	10 (66.7%)	12 (40%)	0.092
ACEI	24 (53.3%)	11 (73.3%)	13 (43.3%)	0.057
AEBS	21 (46.7%)	3 (20%)	18 (60%)	0.011*
BBS	28 (62.2%)	4 (26.7%)	24 (80%)	0.001*
Digital	12 (26.7%)	10 (66.7%)	2 (6.7%)	FEp<0.001*

- χ^2: **Chi square test** - **FE: Fisher Exact** - **t: Student t-test** -**U: Mann Whitney test**
p: p value for comparing between the studied categories
*: Statistically significant at p ≤ 0.05

Table 2: Univariate and multivariate COX regressionanalysis for the parameters affecting mortality

	Univariate		#Multivariate	
	P	HR (95%C.I)	p	HR (95%C.I)
Sex (female)	0.370	0.506(0.114 – 2.245)		
Age (years)	**<0.001***	1.128(1.061 – 1.199)	0.247	1.055 (0.963–1.156)
Smoking	**0.022***	5.726(1.286 – 25.486)	0.767	1.387 (0.160–12.042)
IHD	**0.194**	2.136(0.680 – 6.715)		
HTN	**0.887**	1.086(0.346 – 3.415)		
DM	**0.577**	1.342(0.478 – 3.770)		
Dyslipidemia	**0.445**	1.520(0.519 – 4.451)		
NYHA	**0.051**	64.658(0.999 – 4185.9)		
Systolic BP	**0.658**	0.995(0.973 – 1.017)		
Diastolic BP	**0.834**	1.004(0.966 – 1.043)		
Heart rate (b/m)	**<0.001***	1.094(1.040 – 1.151)	0.075	1.048 (0.995–1.104)
Ejection fraction %	**<0.001***	0.864(0.803 – 0.930)	0.003*	0.889 (0.823– 0.961)
Arrhythmias	**0.005***	4.462(1.572 – 12.662)	0.307	1.960 (0.538–7.134)
Valvular lesions	**0.847**	0.905(0.328 – 2.497)		
Hemoglobin %	**0.064**	0.698(0.478 – 1.021)		
RBS (mg/dl)	**0.424**	0.994(0.981 – 1.008)		
CrCL(ml/min)	**<0.001***	0.892(0.838 – 0.948)	0.480	0.971 (0.896–1.053)
Na (mg/dl)	**0.422**	0.908(0.719 – 1.148)		
K+(mg/dl)	**0.163**	0.389(0.104 – 1.464)		
Copeptin (pmol/L) Day 1	**0.007***	1.437(1.104 – 1.870)		
Copeptin (pmol/L) Day 3	**<0.001***	1.341(1.149 – 1.566)		
Increase Copeptin (pmol/L)	**<0.001***	2.220 (1.500–3.286)	0.097	1.979 (0.884–4.434)

Conclusion

Copeptin is a strong novel biomarker in prognosis of acute heart failure, higher circulating copeptin levels were positively associated with the risk of all-cause mortality and rehospitalization in patients with AHF.

So we recommended using copeptin as a new prognostic biomarker to provide better information not only in decision making for treatment but also in the prediction of clinical outcome.