Copeptin and metabolic syndrome: a systematic review

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Abstract

Background: Copeptin, a reliable marker for vasopressin release, has been associated with cardiometabolic diseases including metabolic syndrome. Objective: To evaluate the association between copeptin and metabolic syndrome in the general population. Methods: We searched in Pubmed, Scopus, EMBASE, and Web of Science databases until March 2021 and included observational studies (cohort studies, cross-sectional, and case-control) reporting the risk or prevalence of having metabolic syndrome in patients with elevated copeptin levels compared to patients without elevated copeptin levels. Risk of bias was evaluated with the New Castle-Ottawa Scale. Meta-analysis was not performed because of the heterogeneity of the copeptin cut-off values. Results: A total of 7 studies (5 cross-sectional, 1 case-control, 1 cohort) were included comprising 11 699 participants. Most of them were performed in the adult community population. Two cross-sectional and the case-control studies found a positive significant association between copeptin and metabolic syndrome. While three cross-sectional and the cohort study found no differences. The case-control study had several methodological limitations, most cross-sectional studies where methodologically adequate and the cohort study had no limitations. Conclusions: Available evidence with regards to this topic is inconsistent. Future studies should aim to use standardized cut-off points so allow for comparison of the findings.

Background

In recent years, the C-terminal sequence of pre-pro vasopressin (Copeptin) has been used as a surrogate marker of vasopressin because of its stability (1,2). Copeptin is related to several cardiometabolic disorders(3-5). This is attributed to the overstimulation of vasopressin receptors (rV) located in different tissues involved in metabolic control (6). Which could explain the development of metabolic syndrome related to elevated Copeptin levels. Thus, copeptin could be an early marker and or prognostic factor for metabolic syndrome.

Discussion

When evaluating the included studies, we found controversy. On the one hand, some cross-sectional studies demonstrated a directly proportional association of copeptin quartiles with metabolic syndrome, whereas other case-control, cohort, and cross-sectional studies found no significant differences. Discrepancies between the results may be due to differences in statistical methods, such as the variables selected for adjustment, the type of analysis that was used, and the cutoff points for copeptin. The fact that the association is seen cross-sectionally suggests that patients with metabolic syndrome may have high copeptin levels, but not necessarily be the cause. The cohort study found prospective association of copeptin with abdominal obesity and diabetes; however, it was not independently associated with metabolic syndrome.

It is important to mention that the studies do not present a standardized cut-off point to divide patients with low or high copeptin, but rather present quartiles, which vary from study to study and make it impossible to perform a meta-analysis.

Table 1. Relationship between copeptin and metabolic syndrome.

Study id	Copeptin categories values	MetS and Copeptin (high vs low)	Mets and copeptin (Q2 vs Q1)	Mets and copeptin (Q3 vs Q1)	Mets and copeptin (Q4 vs Q1)
		Odds Ratio 95% Confindence Interval			
Saleem - 2009 (AA)	Q1 (<5) Q2 (5.0–8.0) Q3 (8-12.7) Q4 (>12.7)	NE	**1.42 (1.05 - 1.93)**	**1.49 (1.07 - 2.06)**	**2.07 (1.45 - 2.95)**
Saleem - 2009 (NHW)	Q1 (<3.32) Q2 (3.32-5) Q3 (5-7.91) Q4 (>7.91)	NE	1.12 (0.79 - 1.59)	**1.79 (1.27 - 2.51)**	**1.74 (1.21 - 2.50)**
Enhörning - 2011	Q1 (<4.59 in men, <2.71 in women) Q2 (4.61–7.13 in men, 2.72–4.24 in women) Q3 (7.14–10.6 in men, 4.25–6.44 in women) Q4 (10.7–428 in men, 6.47–143 in women)	NE	**1.55 (1.25 - 1.93)**	**1.82 (1.47 - 2.25)**	**1.93 (1.57 - 2.39)**
Enhörning - 2013	NR	NE	1.21 (0.85 - 1.72)	1.05 (0.74 - 1.49)	1.34 (0.95 - 1.91)
Then - 2015 (men)	NR	NE	NE	NE	1.13 (0.72 - 1.76)
Then - 2015 (women)	NR	NE	NE	NE	1.11 (0.68 - 1.83)
Vintilă - 2016	Low (0.1-196.4) High (196.5-455.1)	**20 (3.03 - 131.7)**	NE	NE	NE
Canivell - 2017	NR	1.12 (0.74 - 1.69)	NE	NE	NE
Deligözoğlu - 2020	Q1 (<68.7) Q2 (68.7-106) Q3 (107-161) Q4 (162-382)	NE	NE	0.86 (0.22 - 3.28)	0.33 (0.06 - 1.43)

Abbreviations: AA: African Americans, NHW: Non-Hispanic Whites, MetS: metabolic syndrome, SD: standard deviation, NR: not reported, NE: not evaluated. Significative values in bold.

Conclusion

Available evidence with regards to this topic is inconsistent. Future studies should aim to use standardized cut-off points so allow for comparison of the findings.