ASSOCIATION OF ANGIOPOIETIN / TIE2 PLASMA LEVEL AND VEGF SYSTEM WITH PROGRESSION IN GASTROENTEROPANCREATIC NEUROENDOCRINE TUMORS

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INTRODUCTION

Angiopoietins (ANG) -1 and 2, their receptor TIE2, and the vascular endothelial growth fa9ctor (VEGF) are involved in the process of angiogenesis (1-3). However, their role in the pathogenesis and development of gastroenteropancreatic neuroendocrine tumors (GEP-NETs) is not completely understood.

In a previous study (4) of 42 patients with GEP-NET, we observed an elevation of these serum markers, especially in those with metastatic disease (Figure 1).
The objective of this study was to analyze the relationship between plasma levels of the ANG/TIE2-VEGF system in patients with GEP NETs who exhibited progression after 3 years of follow-up.

PATIENTS AND METHODS

26 Patients with GEP-NETs were studied. Primary location of tumors was pancreas (n = 13) and intestine (n = 13). Plasma levels of ANG-1, ANG-2, TIE2 and VEGF were determined by ELISA. We evaluated response to medical and/or surgical treatment using clinical and radiological criteria and patients were assigned to three categories (complete remission, stable disease or progressive response), accordingly. Statistical nonparametric analysis tests was performed.

Figure 1: *Figueroa-Vega et al*; Endocr Relat Cancer 2010; 17:897-908. Serum concentrations of sTie-2 (A), Ang-2 (B), Ang-1 (C), and VEGF (D) in GEP-NET patients with and without metastases, and healthy controls. *p<0,05; ** p<0,01; ***p<0,001
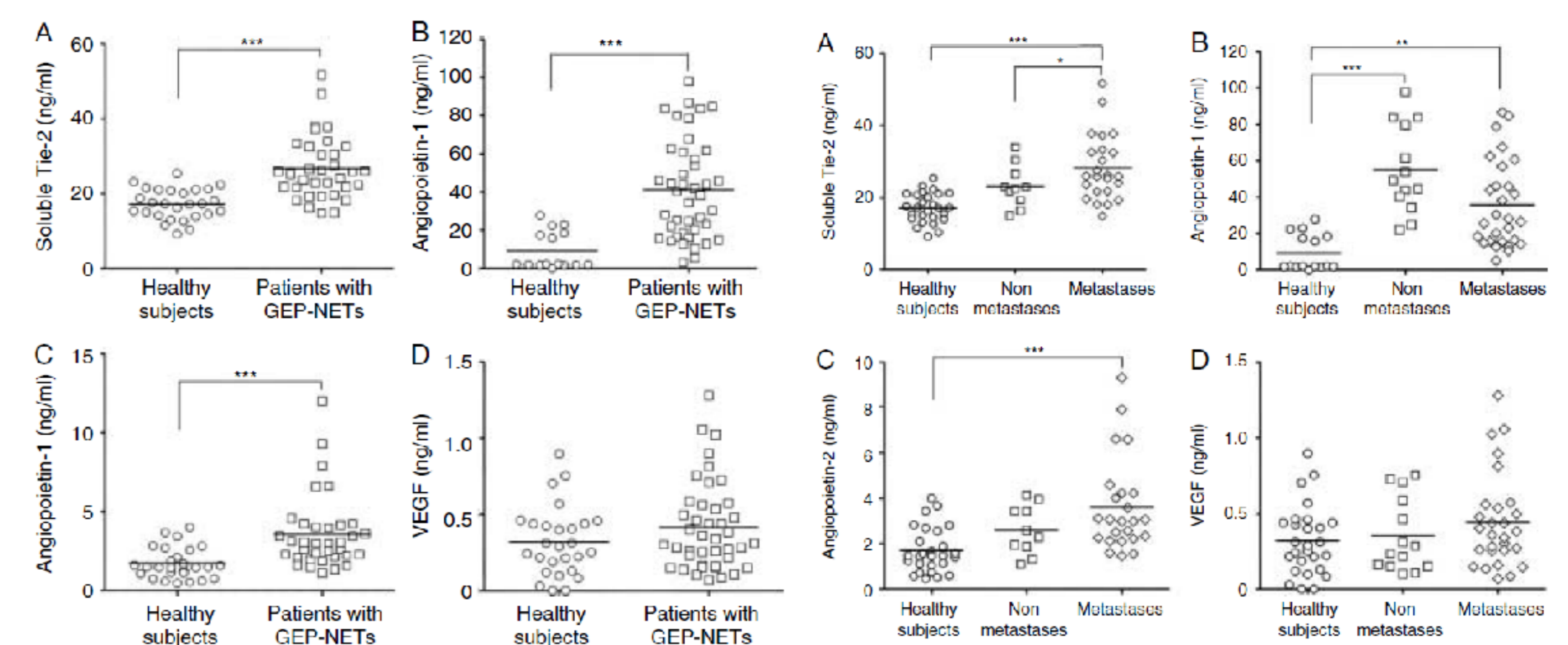
RESULTS

Table 1: General description of patients and their comparison by tumor type

		Primary tumor localization			
		Total	Pancreas	Intestine	p
Patient's Number		26	13	13	
Age (mean, ages)		58	61	55	0.336
Sex feminine (N)		15	9	6	0.234
Size (mean, cm.)		3.6	4.2	3.1	1.000
Metastasis (N)		13	4	9	0.050
RESPONSE TYPE	Complete remission	13	9	4	
	Stable Disease	6	2	5	0,079
	Progressive Disease	7	2	5	
SERUM CONCENTRATIONS	Tie 2 (pg/mL)	26326,85 ± 7080,65	26069,83 ± 7614,83	26547,14 ± 7199,11	0,836
	Ang1 (pg/mL)	50327,58 ± 27357,94	62189,17 ± 20321,44	40160,50 ± 29857,75	0,073
	Ang2 (pg/mL)	4349,64 ± 2975,77	3314,80 ± 1929,33	5236,64 ± 3552,42	0,295
	VEGF (pg/mL)	390,89 ± 234,98	354,11 ± 156,46	422,41 ± 295,83	0,836

Figure 2: Serum concentration of sTIE-2(A), Ang-2 (B), Ang-1 (C) and VEGF (D) in GEP-NET patients. Mean ±2xS.E.M.* p < 0.05
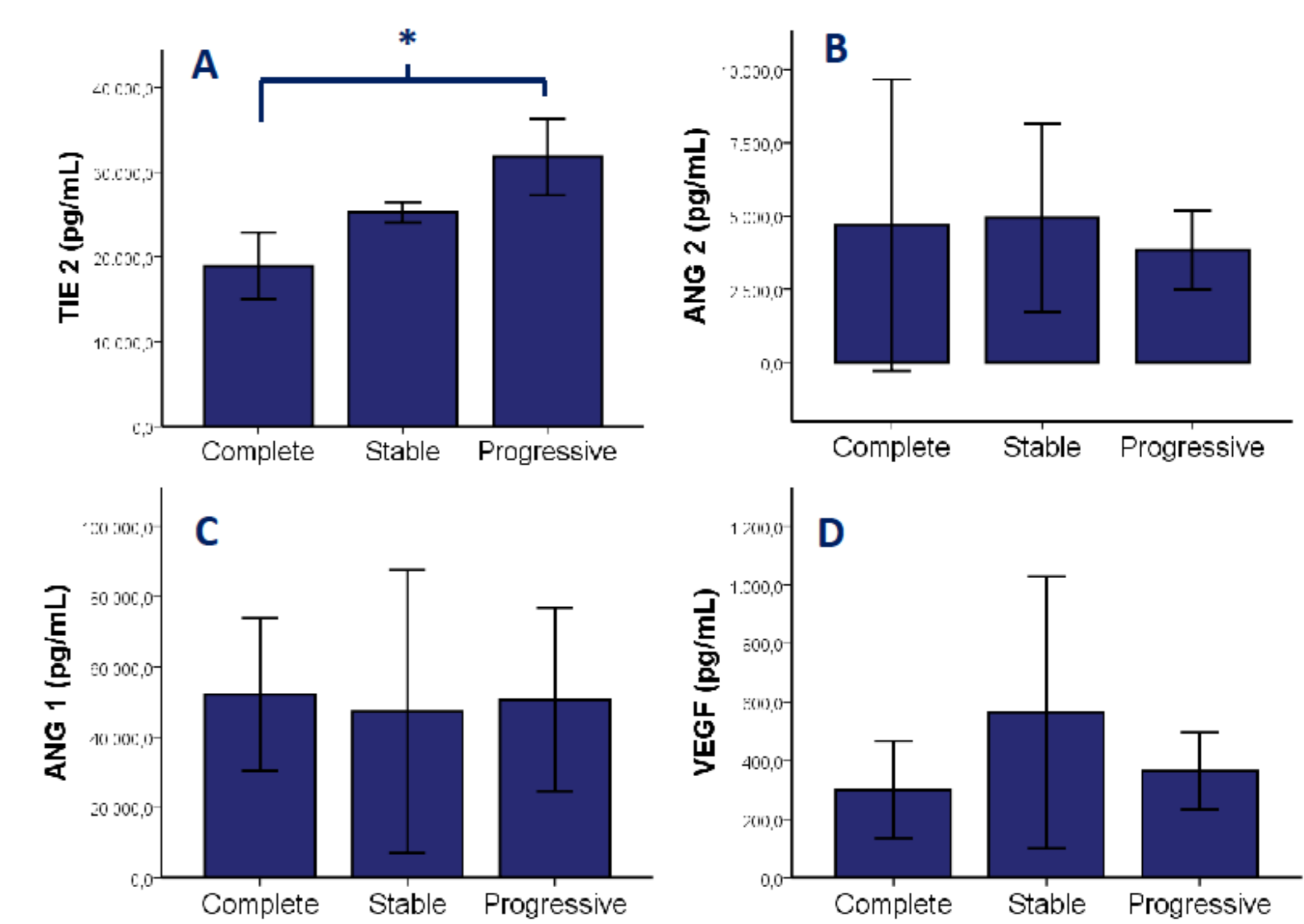
CONCLUSIONS

TIE2 plasma values are higher in patients with GEP-NETs with progressive disease. This suggests a possible involvement of ANG/TIE2 system in the pathogenesis of GEP-NETs and a possible relevance as diagnostic and/or therapeutic target.

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