

# Researching plasma sTWEAK levels in chronic kidney disease stages

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## Objectives:

Recently, we aimed to show that soluble TNF-like weak inducer of apoptosis (sTWEAK) plasma levels are diminished in chronic kidney disease (CKD) patients. Because of previous studies showed that sTWEAK plasma level has been associated with the presence of CKD and cardiovascular disease, we hypothesized that in patients with CKD, sTWEAK levels may relate to the increased prevalence of endothelial dysfunction that usually accompanies the decline of estimated GFR (eGFR).

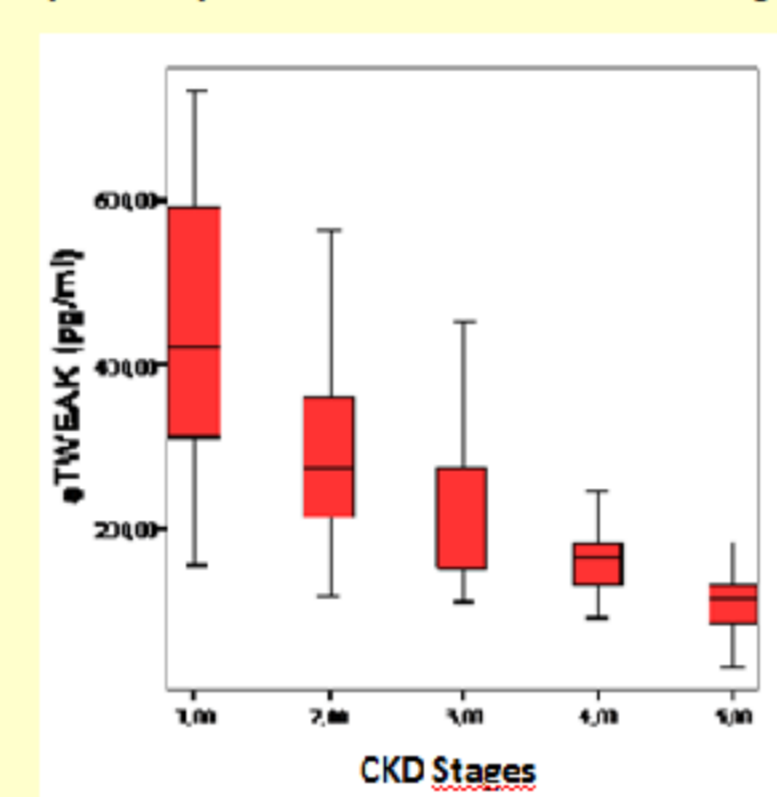
## Methods:

We studied 199 patients with different stages of CKD (51% female; age 51±12 yr), testing the association between sTWEAK plasma levels and CKD stages and the relationship between high-sensitivity C reactive protein (hsCRP), HOMA and sTWEAK concentrations

Comparison of biochemical findings between CKD stages

Parameter	Stage I (n=95)	Stage II (n=95)	Stage III (n=95)	Stage IV (n=95)	Stage V (n=95)	P
eGFR (ml/min/1.73 m <sup>2</sup> )	65.3 ± 3.3	77.5 ± 9.4	48.9 ± 8.1	24.5 ± 8.8	8.9 ± 4.2	<0.001
Proteinuria (mg/day)	130.9 ± 49.7	174.2 ± 77.8	194.6 ± 93.7	188.8 ± 104	221.6 ± 126.9	0.007
SBP (mmHg)	133.2 ± 7.8	138.1 ± 11.1	133.9 ± 8.8	133.9 ± 12.1	137.1 ± 12.2	0.171
DBP (mmHg)	82.6 ± 4.4	84.3 ± 7	84.9 ± 5.5	84.3 ± 4.2	84.3 ± 4.2	0.102
Plasma lipoprotein	5.9 ± 1.4	6.7 ± 1.3	7.4 ± 1.6	7.1 ± 1.6	7.6 ± 1.7	0.002
Plasma glucose (mg/dl)	96.7 ± 27.7	104.1 ± 35.8	102.7 ± 40	106.7 ± 42.9	93.9 ± 17.5	0.344
HOMA-IR	1.7 ± 0.7	1.7 ± 0.7	1.9 ± 1.1	1.9 ± 0.8	1.9 ± 0.8	0.724
Total cholesterol (mg/dl)	204.2 ± 16.4	207.3 ± 16.9	206.7 ± 20	203.2 ± 20	197.1 ± 16.4	0.107
Serum triglyceride (mg/dl)	148.2 ± 14.3	151.1 ± 11.3	151.1 ± 12.2	152.8 ± 13.7	143.4 ± 21.4	0.123
LDL cholesterol (mg/dl)	127.9 ± 16.7	130 ± 16.1	127.9 ± 16.8	127.9 ± 16.2	124.7 ± 22.8	0.484
HDL cholesterol (mg/dl)	43.2 ± 4.6	43.1 ± 5.3	41.2 ± 5.6	42.7	43.2 ± 7.1	0.329
Hemoglobin (g/dl)	12 ± 1.1	11.9 ± 2.3	11.5 ± 1.9	11.1 ± 2.2	10.5 ± 2.1	0.018
Hematocrit (%)	36.3 ± 0.9	36.5 ± 0.3	34.5 ± 0.7	33.8 ± 0.3	32.1 ± 0.4	0.005
Serum albumin (g/dl)	4.0 ± 0.3	3.9 ± 0.4	4.2 ± 0.4	4.0 ± 0.3	3.8 ± 0.3	<0.001
Uric acid (mg/dl)	4.4 ± 0.9	4.7 ± 1.3	6.9 ± 1	7.4 ± 1.1	7.6 ± 1.1	<0.001
Calcium (mg/dl)	8.9 ± 0.4	8.7 ± 0.6	8.3 ± 0.6	8.1 ± 0.4	8.0 ± 0.3	<0.001
Phosphate (mg/dl)	4.2 ± 0.5	4.4 ± 0.8	4.6 ± 0.7	5.9 ± 1.4	6.9 ± 1.6	<0.001
Parathyroid (pg/ml)	59.3 ± 12.8	70.9 ± 31.2	104.3 ± 41.1	172.9 ± 38.9	296.2 ± 38.9	<0.001
hsCRP (mg/l)	9.2 ± 2.4	12.2 ± 2.1	17.2 ± 4.7	19.1 ± 8.4	31.2 ± 11.8	<0.001
sTWEAK (pg/ml)	438.6 ± 103.4	297.1 ± 110.6	237.9 ± 103.9	176.1 ± 72.4	110.2 ± 34.9	<0.001

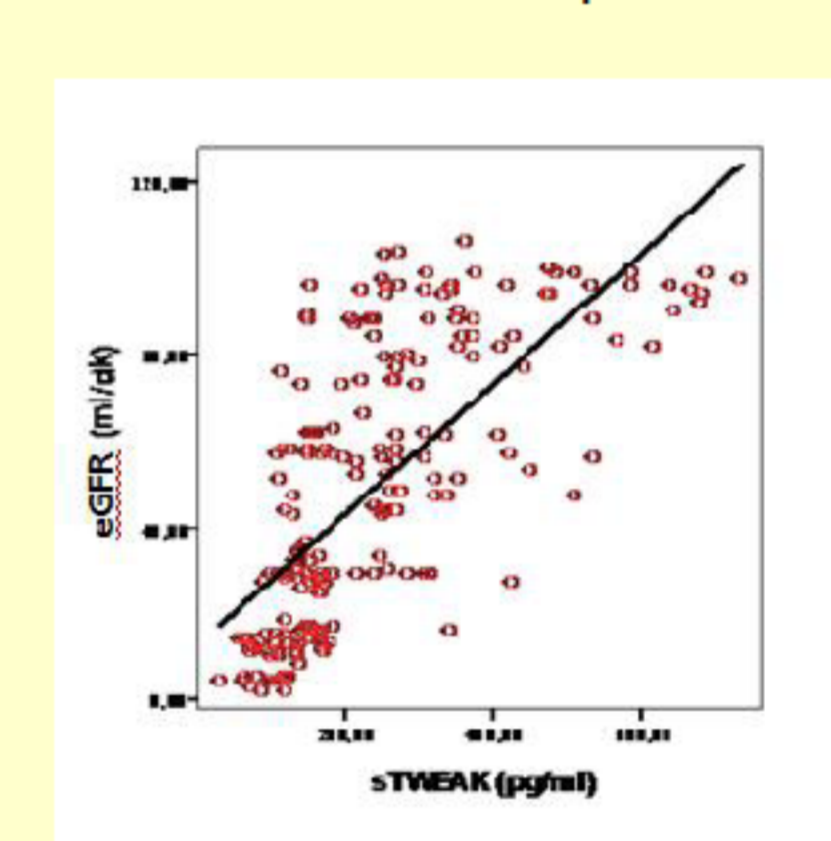
Comparison of plasma sTWEAK level between CKD stages



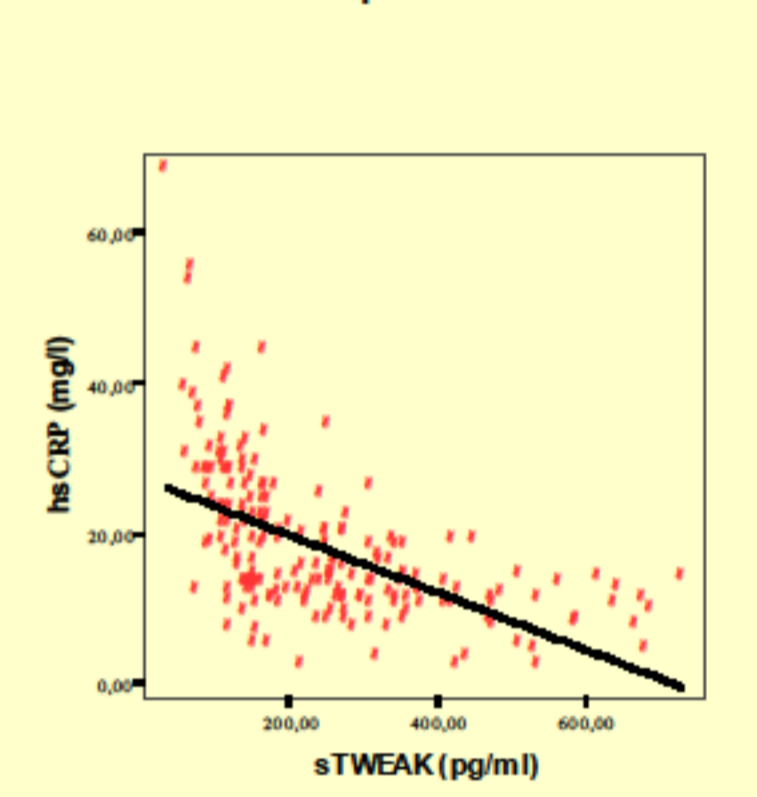
Correlation analysis of parameters and plasma sTWEAK in CKD stages

Parameter	r	P
Age	-0.074	0.258
Gender	0.113	0.112
BMI (kg/m <sup>2</sup> )	0.009	0.105
eGFR (ml/min/1.73 m <sup>2</sup> )	0.756	<0.001
Serum albumin (g/dl)	0.147	0.628
Proteinuria (mg/day)	-0.213	0.003
SBP (mmHg)	-0.39	0.238
DBP (mmHg)	-0.122	0.007
Hemoglobin (g/dl)	0.076	0.287
Hematocrit (%)	0.112	0.112
Plasma lipoprotein	-0.046	0.521
Plasma glucose (mg/dl)	-0.115	0.107
HOMA-IR	-0.138	0.052
Total cholesterol (mg/dl)	-0.008	0.929
Serum triglyceride (mg/dl)	-0.056	0.431
LDL cholesterol (mg/dl)	-0.05	0.48
HDL cholesterol (mg/dl)	-0.007	0.92
Uric acid (mg/dl)	-0.004	0.981
Calcium (mg/dl)	0.423	<0.001
Phosphate (mg/dl)	-0.562	<0.001
Parathyroid (pg/ml)	-0.146	<0.001
hsCRP (mg/l)	-0.652	<0.001

Correlation between eGFR and plasma sTWEAK levels



Correlation between plasma sTWEAK levels and hsCRP



eGFR: estimated Glomerular filtration rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, hsCRP: High sensitivity C reactivity protein, sTWEAK: soluble TNF-like weak inducer of apoptosis

BMI: Body mass index, eGFR: estimated Glomerular filtration rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, hsCRP: High sensitivity C reactivity protein

## Results:

A gradual decrease in sTWEAK was observed as eGFR decreased. Soluble TWEAK plasma levels were diminished in all stages of CKD and strongly correlated with eGFR.

Negative correlation between sTWEAK and hsCRP ( $p < 0.001$ ,  $r = -0.652$ ) and positive correlation between sTWEAK and eGFR ( $p < 0.001$ ,  $r = 0.756$ ) were found. No significant correlation was found between sTWEAK and HOMA-IR ( $p > 0.05$ ).

## Conclusions:

A decline in eGFR is accompanied by gradual reductions in sTWEAK plasma levels. Because sTWEAK strongly and independently correlated with CRP, our study suggests novel links between sTWEAK and endothelial dysfunction in patients with CKD.

## References:

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- 3-Blanco-Collo, L.M., Martín-Ventura, J.L., Muñoz-García, B., Orbe, J., et al. Identification of soluble tumor necrosis factor-like weak inducer of apoptosis (sTWEAK) as a possible biomarker of subclinical atherosclerosis. *Arterioscler Thromb Vasc Biol.* 2007;27:916-22.