

# ENDOTHELIAL dysFUNCTION AND CARDIOVASCULAR RISK IN PATIENTS WITH CRHONIC KIDNEY DISEASE

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## Objectives:

Cardiovascular (CV) diseases are the leading causes of morbidity and mortality in patients with chronic kidney disease (CKD) that encompass the mildest degrees of renal impairment. Endothelial dysfunction (ED) represents the earliest abnormality in the development of vascular disease linked to CV diseases. Fibroblast growth factor 23 (FGF-23) a recently described regulator of phosphate metabolism increase early in CKD patients and was associated with increased CV events in this population. In this study we aimed to examine the relationship between FGF-23 serum levels and endothelial function in pre-dialysis CKD patients in stages 1 to 5.

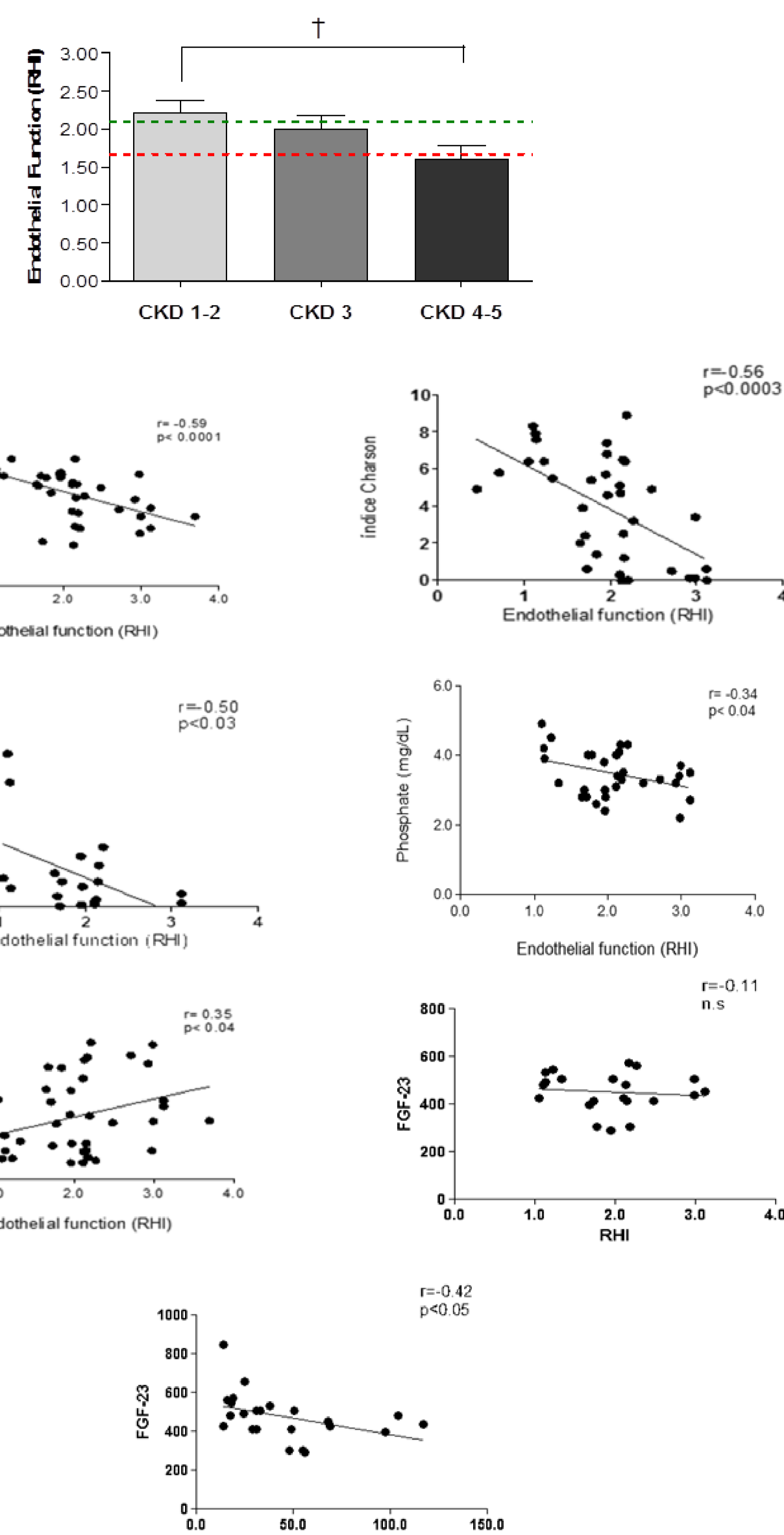
## Methods:

We examined 43 CKD patients followed-up in our outpatient clinic. Patients were distributed in the 5 stages of CKD according to the GFR calculated by CKD-EPI formula (CKD stage 1-2 [n=16, M37%, age 48.6±3.2], CKD stage 3 [n=14, M33%, age 58.0±4.1], CKD stage 4-5 [n=13, M33%, age 59.8±4.0]. Renal function, blood pressure, proteinuria, phosphate serum levels and a validated comorbidity index (Charlson Index) were evaluated in the studied population. Intact FGF-23 levels were assessed by ELISA (Immupics, Inc.). Endothelial function was assessed by peripheral arterial tonometry (Endo-Pat 2000) where lower reactive hyperaemia index (RHI) values correspond to greater ED.

## Results:

	CKD stage 1-2 (n=16)	CKD stage 3 (n=14)	CKD stage 4-5 (n=13)
<b>Demographic data</b>			
Age (years)	43.4 6.5	54.9 6.4	67.8 6.9*#
Male (%)	20	50*	50†
Height (cm)	165.2 5.1	159.4 3.9	164.1 3.2
Weight (kg)	79.6 3.6	71.1 6.9	72.6 3.7
BMI (kg/m <sup>2</sup> )	29.3 1.9	27.8 2.2	27.1 1.2
<b>Clinical Data</b>			
High BP (%)	80	88	100#
DM (%)	20	13	50#
<b>Analytical data</b>			
P creat (mg/dL)	1.1 0.1	1.7 0.1*	4,6 5,8#
P urea (mg/dL)	61.8 9.2	82.0 8.3	120.0 14.6†
U Prot/Creat ratio	626.8 218.3	617.1 132.5	1630.7 766.4**
Calcium (mEq/L)	4.8 0.0	5.0 0.1	4.8 0.1
Phosphate (mg/dL)	3.3 0.2	3.3 0.2	4.0 0.1#
PHT (pg/mL)	34.0 3.2	110.3 28.7	177.0 42.5†
OH-25-Vit D (ng/mL)	21.3 5.9	23.6 2.5	23.1 4.1
Alkaline phosphatase (U/L)	68.6 4.3	95.7 14.6	119.8 17.8†
Endothelial function (RHI)	2.5 0.4	2.4 0.3	2.0 0.4†

\*Significantly different between stage 1-2 vs 3;  
† Significantly different between stage 1-2 vs 5-4  
# Significantly different between stage 3 vs 5-4;



## Conclusions:

In summary, our results provide evidence favoring the view that endoPAT 2000, a non-invasived method for evaluation of endothelial function, can provide clinically important information to identify vulnerable patients, and stratify cardiovascular risk in this population. Our results also suggest that serum phosphate and FGF-23 levels promote vascular disease through distinct mechanisms.

## References:

- 1) Ronen Rubinshtein, Jeffrey T. Kuvin, Morgan Soffler, Ryan J. Lennon, Shahar Lavi, Rebecca E. Nelson, GERALYN M. PUMPER, Lilach O. Lerman, and Amir Lerman. Assessment of endothelial function by non-invasive peripheral arterial tonometry predicts late cardiovascular adverse events. *European Heart Journal* (2010) 31, 1142–1148
- 2) Naomi M. Hamburg, Michelle J. Keyes, Martin G. Larson, Ramachandran S. Vasan, Renate, Schnabel, Moira M. Pryde, Gary F. Mitchell, Jacob Sheffy, Joseph A. Vita and Emelia J. Benjamin. Cross-Sectional Relations of Digital Vascular Function to Cardiovascular Risk Factors in the Framingham Heart Study *Circulation*. 2008;117:2467-2474
- 3) John E. Deanfield, Julian P. Halcox and Ton J. Rabelink. Endothelial Function and Dysfunction: Testing and Clinical Relevance. *Circulation*. 2007;115:1285-1295
- 4) Michael E. Widlansky, MD, Noyan Gokce, MD, FACC, John F. Keaney, JR, MD, FACC, Joseph A. Vita, MD, FACC. Boston, Massachusetts. The Clinical Implications of Endothelial Dysfunction. *Journal of the American College of Cardiology* Vol. 42, No. 7, 2003

