

LEVELS OF SERUM ANGIOTENSIN-CONVERTING ENZYME TYPE 2 (ACE2) ARE ASSOCIATED WITH INCREASED INSULIN RESISTANCE INDEPENDENTLY OF ALBUMINURIA IN TYPE 2 DIABETES.

A Chacon*, MJ Soler**, J Escalada*, M. Riera**, JM Mora***, N Garcia-Fernandez***.

*Department of Endocrinology, ***Department of Nephrology, Clínica Universidad de Navarra. Spain. **Department of Nephrology, Hospital del Mar. Barcelona. Spain.

Introduction

- Angiotensin-converting enzyme type 2 (ACE2) is a novel ACE homologue, which has actions that counterbalance Ang II: vasodilatation, antiproliferation, and apoptosis functions. In the context of diabetes, ACE2s implication in cardiovascular and renal pathophysiology has become particularly important in recent years.
- Recent studies associate ACE2 with the presence of albuminuria in patients with diabetes indicating that ACE2 may participate as a compensatory mechanism. On the other hand, clinical studies have reported higher levels of ACE2 in insulin-resistant subjects. In patients with type 2 diabetes (T2D), increased urinary albumin excretion is strongly associated with insulin resistance.

Objective

The aim of this study is to evaluate the role of ACE2 in patients with T2D keeping in mind the association between albuminuria and insulin resistance.

Patients and Methods

- We performed a cross-sectional and case-control study. 61 patients with DM2 and an estimated glomerular filtration rate by MDRD greater than 60 mL/min/1,73m² were studied.
 - 31 patients in the control group had category A1 of albuminuria;
 - and 30 patients in the case group had category A2 of albuminuria (urine albumin/creatinine ratio (ACR): 30-300 mg/g).
- Age, gender, diabetes duration, renin-angiotensin system inhibitors, different metabolic factors (as fasting glucose, body composition data, lipidic profile, blood pressure) and vascular disease history were documented. **Serum ACE2 activity** was measured in all patients. Insulin resistance was assessed by homeostasis model assessment for **insulin resistance (HOMA-IR) index and urinary albumin excretion by urine ACR**. SPSS 20.0 software was used for statistical analysis.

Results

Table 1 shows correlations between serum ACE2 and various metabolic risk factors. The image shows the correlation between ACE2 and HOMAR.

	Serum ACE2 (FUR/UI/h)	
	r	p
Age	0.13	0.919
BMI	0.443	0.000
Waist circumference	0.468	0.001
CUN-BAE	0.264	0.040
Fasting glucose	0.325	0.011
Fasting insulin	0.433	0.002
HOMA-R	0.586	0.000
HDL-c	-0.215	0.096
LDL-c	0.111	0.393
Triglycerides	0.267	0.037
CRP	0.065	0.617
SBP	0.226	0.082
DBP	0.474	0.013
ACR	0.217	0.093
Cr	0.190	0.142

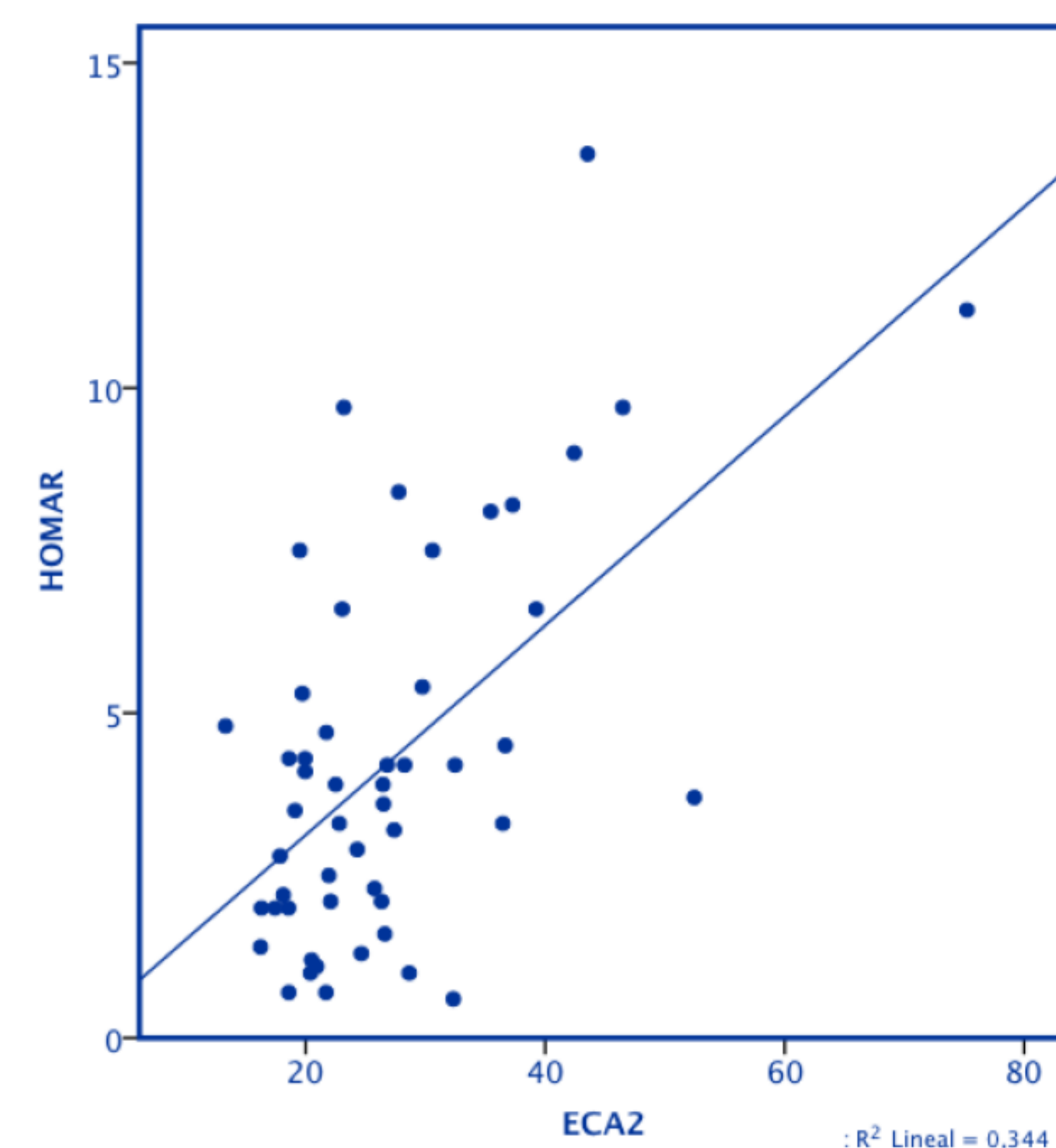


Table 2 shows a lineal regression model for ACE2 level

	T (HR)	P value
Age	-0.06	0.778
BMI	0.328	0.369
HOMA-R	1.639	0.019
Triglycerides	0.024	0.340
CRP	-0.495	0.733
SBP	0.009	0.934
DBP	0.075	0.702
ACR	0.005	0.840

Table 3 shows the risk of Albuminuria. Logistic regression model. (OR)

	OR	P value
Age	0.886	0.175
BMI	0.997	0.987
HOMA-R	2.22	0.029
CRP	4.925	0.170
SBP	1.129	0.052
DBP	0.864	0.142
eGFR	0.987	0.648
HbA1c	0.907	0.841
ACE2	1.108	0.282

* BMI, body mass index; CUN-BAE, CUN-BAE equation, (a validated predictive equation to estimate body fat percentage); HOMA-R, homeostasis model assessment of insulin resistance; LDL-c, low-density lipoproteins cholesterol; CRP, C reactive protein; SBP, systolic blood pressure; DBP, diastolic blood pressure; ACR, albumin-to-creatinine ratio; Cr, serum creatinine concentration; eGFR, estimated glomerular filtration rate.

Conclusions

- We found that serum **ACE2 levels in DM2 patients are associated with insulin resistance and not with the presence of microalbuminuria after adjusting with different metabolic factors.**
- We consider that **insulin resistance could be considered as a confounding factor** in the role that has been granted to the ACE2 as a predictor of microalbuminuria in patients with T2D. However, future studies are needed to confirm this result.
- Future studies are needed to confirm these results.

