

# DETERMINANTS OF GLOMERULAR FILTRATION RATE DECLINE IN TYPE 2 DIABETES

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## BACKGROUND

- Diabetic nephropathy develops in 40%–60% of individuals with type 2 diabetes (DM2) and it is characterized by a progressive and persistent decline in kidney function
- The course of GFR is very complex and heterogeneous, mainly depending on individual and disease specific conditions.

## OBJECTIVES

- To study which clinical factors were associated with the GFR annual decline

## METHODS

- We studied all patients with CKD and DM2 (n=128) that were referred to our ambulatory clinic in 2012 and followed for a mean 3.2±1.2 years.
- Annual GFR values were calculated for each patient by MDRD formula, and % GFR annual decline was then calculated.
- For the purpose of this study we considered:
  - Degree of albuminuria according to KDIGO guidelines (A1 to A3).
  - % GFR annual decline ≤-4% as **rapid decliner** (RD, n=67)
  - % GFR annual decline >-4% as **non-rapid decliners** (NRD, n=61)

- Significant **risk factors** for RD status were explored by multivariable logistic regression model, using a backward elimination method

✓ Principal variables included:

age	sex	smoker
coronary heart disease	cerebrovascular disease	congestive heart failure (CHF)
diabetes treated with insulin	CKD stage	albuminuria status(AlbU)
vascular disease	BMI	haemoglobin A1C (HbA1c)
diabetic retinopathy	Years of DM2	number of antihypertension drugs
anticoagulation	Anti-agregation	diuretic use
phosphorus levels (PO), Calcium (Ca)	Haemoglobin (Hg)	angiotensin converting enzyme inhibitors (ACEi)
parathyroid hormone (PTH)	transferrin saturation	angiotensin II receptor antagonist (ARA)

## RESULTS

- Cohort mean age was 68.8±12.1 years
- 58% were man
- Median baseline eGFR (± IQR) was 38.8 (28.8-54.4) ml/min/1.73m<sup>2</sup>

- Significant risks for GFR decline were (considering all variables): smoker, A3, treated with insulin and with 3-4 antihypertension drugs.

Table 1.	NRD eGFR decline >-4% N=61 (48%)	RD eGFR decline ≤-4% N=67 (52%)	P
AlbU mg/g, median (IQR)	78 (8-364)	723 (71-2360)	<0.001
Pcreat mg/dl, median (IQR)	1.49 (1.20-2.01)	1.75 (1.10-2.17)	0.585
MDRD ml/min, median (IQR)	40.5 (28.8-53.3)	38.1 (28.8-59.4)	0.964
eGFR decline ml/min/y, median (IQR)	0.7 (-0.9-3.1)	-4.5 (-8.1-(-2.8))	<0.001
eGFR decline %/y, median (IQR)	2.0 (-2.0-9.4)	-11.2 (-18.2-(-7.7))	<0.001
Female, n (%)	31 (51)	23 (34)	0.059
Age, average±SD	71.4±11.9	66.5±11.9	0.022
Years of DM2, average±SD	10.5±1.4	9.6±1.2	0.879
BMI, average±SD	29.2±5.5	29.3±5.7	0.900
HbA1c, average±SD	7.1±1.4	7.2±1.6	0.802
Albumin, average±SD	4.2±0.4	4.0±0.6	0.008
K, average±SD	4.8±0.6	4.6±0.6	0.172
Hg, average±SD	12.3±2.4	12.3±1.9	0.901
Transferrin saturation, average±SD	21±10	23±9	0.242
PTH, average±SD	114±84	132±123	0.429
Ca, average±SD	2.38±0.13	2.38±0.16	0.991
PO, average±SD	1.13±0.23	1.24±0.28	0.021
Number of antihypertension drugs, n (%)			0.007
0	7 (12)	2 (3)	
1-2	50 (82)	52 (78)	
3-4	4 (7)	13 (19)	
CKD stage, n (%)			0.379
1	3 (5)	9 (13)	
2	8 (13)	7 (10)	
3	33 (54)	31 (46)	
4	16 (26)	20 (30)	
5	1 (2)	0	
AlbU, n (%)			0.001
A1	17 (35)	8 (14)	
A2	16 (33)	14 (24)	
A3	16 (33)	36 (62)	
Coronary heart disease, n (%)	18 (30)	18 (27)	0.740
CHF, n (%)	21 (34)	24 (36)	0.869
Arrhythmia, n (%)	17 (28)	13 (19)	0.259
Cerebrovascular disease, n (%)	9 (15)	16 (24)	0.193
Vascular disease, n (%)	10 (16)	16 (24)	0.293
Diabetic retinopathy, n (%)	14 (23)	31 (46)	0.006
Smoker, n (%)			0.003
Non smoker	44 (77)	31 (50)	
Ex-smoker	10 (18)	22 (36)	
Active smoker	3 (5)	9 (15)	
Diabetes treated with insulin, n (%)	18 (30)	35 (52)	0.009
ACEi, n (%)	26 (43)	25 (37)	0.540
ARA, n (%)	23 (38)	31 (46)	0.327
ACEi±ARA	47 (77)	54 (81)	0.623

Table 2.	OR	95% CI	P
Number of antihypertension drugs, n (%)			
0	Ref.		
1-2	3.56	0.46-27.61	0.224
3-4	16.96	1.41-204.0	0.026
AlbU, n (%)			
A1	Ref.		
A2	1.62	0.46-5.68	0.452
A3	4.17	1.30-13.45	0.017
Diabetes treated with insulin, n (%)	2.39	1.03-5.53	0.043
Smoker, n (%)			
Non smoker	Ref.		
Ex-smoker	3.66	1.38-9.71	0.009
Active smoker	6.80	1.31-35.24	0.022

- Considering a %GFR annual decline as a continuous variable, we found that the presence of diabetic retinopathy (RET), A3 vs A1+2 and insulin-treated DM were associated with higher decline rates.
- When we group these risk factors we have a significant correlation with the GFR annual decline (Figure 1).

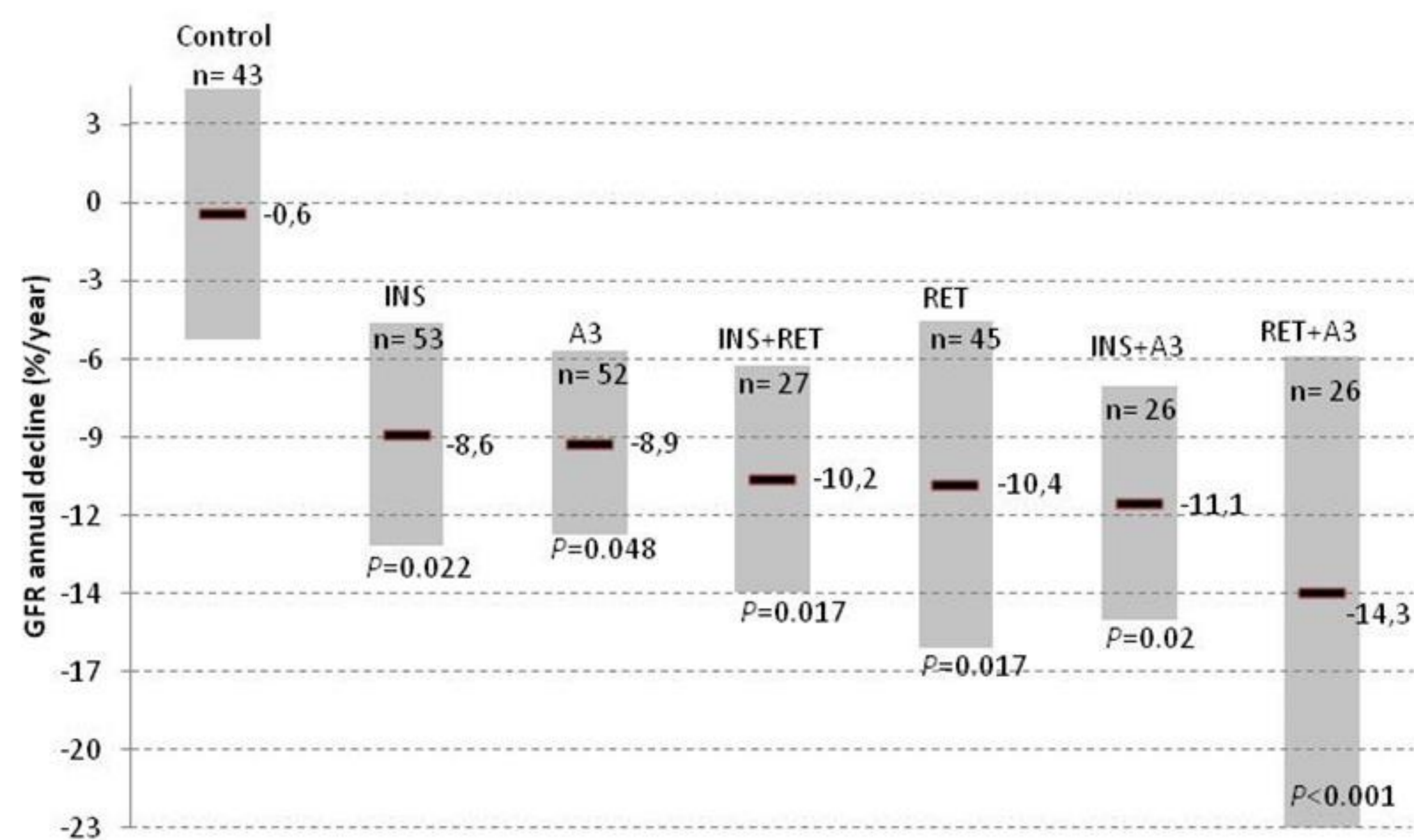


Figure 1. Comparison of GFR annual decline (%/year) between control subjects (with no diabetic retinopathy, diabetes treated without insulin and A1 or A2 status) and subjects with different risk factors combinations. Mean and confidence intervals ranges are given. RET- diabetic retinopathy; INS- diabetes treated with insulin

## CONCLUSION

Knowledge of main risk factors for GFR decline is of clinical importance to improve management in diabetic patients with risk for kidney disease. Smokers, subjects with a higher number of antihypertension drugs, higher degree of albuminuria, diabetic retinopathy and the need of insulin had a faster rate of glomerular filtration rate decline.