



Diabetes onset before or after the age of 65—does it affect the progression of renal and cardiovascular diseases in the elderly patient?

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Type 2 diabetes (T2D) is common in the elderly and more than half of the people with diabetes are over 65 years old.^[1,2] Elderly diabetic patients have a higher frequency of hypertension, coronary artery disease and chronic kidney disease than non-diabetic elderly patients and the risk of these complications increases with patient age, duration of the diabetes and glycated hemoglobin values. Besides the known classical factors of renal disease progression, can one suppose that the age of onset of diabetes may also affect renal disease progression in elderly diabetic patients? The aim of this study was to determine clinical and biological parameters at admission and throughout evolution of elderly diabetic patients with T2D diagnosed before *vs.* after age 65 years.

This is a prospective study started in January 2009 and conducted at the Reference Center for Chronic Diseases in Oujda, Morocco (Eastern Morocco). The Ethics Committee of Morocco's Mohammed V University in Rabat approved the study protocol (University Mohamed V Souissi, Rabat). Verbal informed consent was required from all participants. Inclusion criteria targeted patients who were aged 65 years and older with confirmed T2D at the time of enrollment of the study, and who had been regularly followed in nephrology consultation for at least 36 months. Cardiac events were defined by history of angina, myocardial infarction, heart failure and/or coronary revascularization. Two groups of patients were studied according to age at the time of diabetes diagnosis (before age 65 years *vs.* after age 65 years). Excluded from the study were T2D patients who had conditions other than diabetes and hypertension capable of altering renal function.

Data were analyzed using the Statistical Package for So-

cial Sciences version 13.0 (SPSS, Inc., Chicago, IL). Comparison of quantitative variables between paired groups was performed by analysis of the Student's *t* test. Comparison of qualitative variables between paired groups was performed using the Chi-Square test. All *P* values were two-sided and *P* < 0.05 was considered statistically significant.

In a total cohort of 637 T2D patients with regular follow-up in nephrology, 368 were elderly, representing an incidence of 57% of all diabetic patients. 20.5%, 59.2% and 20.3% of all patients were negative for albuminuria (< 30 mg/day), microalbuminuria (30–300 mg/d) and macroalbuminuria (> 300 mg/d) respectively. Table 1 shows the comparison of clinical and biological parameters in the two groups of elderly diabetic patients according to the age of onset of diabetes, both at the time of enrollment in the study and at the end of the study. In multivariate analysis and adjusting for diabetes duration, the independent factors were as follows: for terminal chronic kidney disease, a low estimated glomerular filtration rate (eGFR, OR = 0.73, 95% CI: 0.62–0.86, *P* ≤ 0.001) and albuminuria (OR = 0.10, 95% CI: 1.000–1.002, *P* = 0.03); for rapid progression of renal disease a low eGFR (OR = 0.90, 95% CI: 0.88–0.92, *P* ≤ 0.001) and albuminuria (OR = 1.00, 95% CI: 1.000–1.002, *P* = 0.01) and for cardiac disease a history of cardiac events (OR = 20.2, 95% CI: 8.6–547.4, *P* ≤ 0.001).

Approximately one third of elderly T2D patients are positive for albuminuria and 15% have a low eGFR.^[3,4] In our series, more than two thirds of patients were positive for albuminuria and one third had a low eGFR. This high incidence may be partly explained by the selective method of recruitment and partly by the high incidence of hypertension. The prevalence of hypertension varies from 60% to 82% in elderly patients with T2D according to the different series.^[5]

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Table 1. Comparison of clinical and biological characteristics in the two groups of elderly diabetic patients according to the age of onset of type 2 diabetes (*n* = 368).

	All patients (<i>n</i> = 368)	Elderly patients with diabetes onset > 65 years (<i>n</i> = 104)	Elderly patients with diabetes onset < 65 years (<i>n</i> = 264)	<i>P</i> -value
At the time of enrollment of the study				
Mean age, yrs	74 ± 7	80 ± 6	71 ± 5	< 0.001
Age, yrs				
< 45	25 (6.8%)	-	25 (9.5%)	
45–54	108 (29.6%)	-	110 (41.7%)	
55–64	128 (35.1%)	-	129 (48.9%)	< 0.001
65–74	83 (22.7%)	83 (79.8%)	-	
> 75	21 (5.8%)	21 (20.2%)	-	
Age at onset of diabetes, yrs	58 ± 9	70 ± 4.5	53 ± 6.5	< 0.001
Duration of diabetes, yrs	16 ± 7.5	10 ± 4.5	18 ± 7.4	< 0.001
Females	233 (63.3%)	60 (57.7%)	173 (65.5%)	0.15
Body mass index, kg/m ²	28.4 ± 4.5	27.1 ± 3.9	29 ± 4.5	< 0.001
Obesity	122 (33.4%)	22 (21.2%)	101 (38.4%)	0.002
Family history of diabetes	220 (60.3%)	44 (42.3%)	179 (67.8%)	< 0.001
History of cardiac events	51 (13.9%)	18 (17.3%)	33 (12.5%)	0.22
History of hypertension	233 (63.8%)	60 (57.7%)	173 (66.3%)	0.14
Hypertension	164 (44.9%)	36 (34.6%)	128 (48.5%)	0.01
Diabetic retinopathy	163 (44.3%)	29 (27.9%)	134 (50.8%)	< 0.001
Diabetic neuropathy	169 (46%)	28 (26.9%)	141 (53.6%)	< 0.001
Smokers	36 (10%)	11 (10.6%)	25 (9.8%)	0.81
Glomerular filtration rate estimated by MDRD, mL/min per 1.73 m ²	79 (57–96)	82 (58–100)	69 (52–89)	0.02
Glomerular filtration rate estimated by MDRD < 60 mL/min per 1,73 m ²	109 (29.6)	33 (31.7)	76 (28.8)	0.57
Albumin excretion rate, mg/day	74 (36–227)	78 (40 – 248)	64 (35–142)	0.04
Total cholesterol, g/L	1.99 ± 0.43	1.91 ± 0.41	2.01 ± 0.43	0.04
LDL-cholesterol target, g/L	1.22 ± 0.35	1.17 ± 0.35	1.19 ± 0.35	0.81
Hemoglobin, g/dL	12 ± 1.5	13.3 ± 1.5	12.8 ± 1.6	0.30
Hb _{A1C} < 7.5%	170 (46.2%)	57 (54.8%)	113 (42.8%)	0.02
At the end of the study				
Mean length of follow-up, months	37 ± 9	33 ± 11	35 ± 17	0.57
Use of ACEi or ARBs	329 (89.4%)	91 (87.5%)	238 (90.2%)	0.46
Use of statin	147 (39.9%)	35 (33.7%)	112 (42.4%)	0.15
Use of > 2 hypertensive drugs	147 (39.9%)	37 (35.6%)	110 (41.7%)	0.34
Use of insulin	236 (64.1%)	50 (48.1%)	186 (70.5%)	< 0.001
Use of oral antidiabetic drug	256 (70.1%)	79 (76%)	177 (67%)	0.09
Glomerular filtration rate estimated by MDRD, mL/min per 1.73 m ²	79 (57–96)	80 (54–95)	70 (52–87)	0.05
Rapid progression (eGFR > 5 mL /min per 1.73 m ² per year)	110 (30.1%)	31 (29.8%)	79 (29.9%)	0.93
End stage renal disease (eGFR < 15 mL/min per 1.73 m ²)	16 (4.3%)	1 (1%)	15 (5.7%)	0.03
Cardiac events occurred	59 (16%)	15 (14.4%)	44 (16.7%)	0.59
Hb _{A1C} target (< 7.5%)	165 (44.8%)	60 (57.7%)	105 (39.8%)	0.002
Hypertension	146 (39.7)	28 (26.9)	118 (44.7)	0.002
Albumin excretion rate, mg/day	70 (35–219)	72 (25–176)	45 (19–130)	0.03
Total cholesterol, g/L	1.91 ± 0.39	1.87 ± 0.38	1.91 ± 0.40	0.29
LDL-cholesterol target, g/L	1.18 ± 0.33	1.16 ± 0.34	1.19 ± 0.33	0.53

Data are presented as *n* (%), mean ± SD or median (IQR) unless other indicated. Hypertension was defined by systolic blood pressure ≥ 140 and/or diastolic blood pressure ≥ 90 mmHg; ACEi: angiotensin converting enzyme inhibitors; ARBs: angiotensin receptor blockers; eGFR: estimated glomerular filtration rate; IQR: interquartile range; LDL: low density lipoprotein cholesterol; MDRD: modification diet in renal disease.

On admission, diabetic retinopathy, diabetic neuropathy, poor glycemic control, poor blood pressure control and increased cholesterol were higher among T2D patients diagnosed before the age of 65 years. For the most part, this may be explained by the duration of diabetes, which was greater in this group of patients. However, after an average follow-up of 36 months, rapid progression of renal disease and the occurrence of cardiac events were identical in the two groups of patients, despite the difference observed between the two groups at the end of follow-up regarding the incidence of hypertension and poor glycemic control.

In conclusion, the age at diagnosis of diabetes after the age of 65 does not seem to affect the progression of renal and cardiovascular disease, which in our series, remain mainly related to low eGFR and smoking. Finally, low eGFR and albuminuria remain powerful independent factors for progression of renal disease at any age of diabetes onset in the elderly diabetic patient.

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