Factors Related to Progression to Macroalbuminuria in Type 1 Diabetic Children with microalbuminuria

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Introduction

Diabetic nephropathy is the leading cause of chronic kidney disease in patients starting renal replacement therapy. Microalbuminuria is an early marker of structural renal disease. Microalbuminuria can regress to normoalbuminuria or progress to macroalbuminuria. Therefore, it is imperative to find out the prognostic factors that are associated with progression to macroalbuminuria. Recently, HbA1c variability has recently been idetified as a risk factor ofmicrovascular complications in type 1 diabetes.

Objectives

The aims of this study was to investigate the frequency of "regression to normoalbuminuria" or "progression to macroalbuminuria" and analyze the effect of mean and variability of HbA1c on progression to macroalbuminuria in children and adolescents.

Material and Methods

This is a retrospective study of 38 patients with type 1 diabetes and microalbuminuria. Among 38 subjects, patients who developed macroalbuminuria were classified as progression group and others were classified as nonprogression group, which was further subclassified into regression group and persistence group. HbA1c was collected from 2 years prior to the first episode of microalbuminuria to the first episode of macroalbuminuria for the progression group and to the last follow up date for nonprogression group. Mean HbA1c and HbA1c variability were calculated in both periods: 2 years prior to onset of microalbuminuria (Pre-A1c(mean), Pre-A1c(variability) and after onset of microalbuminuria (Post-A1c(mean), Post-A1c(variability). Sex, age, pubertal status, blood pressure, total cholesterol were collected at diagnosis of microalbuminuria. The use of angiotensin converting enzyme inhibitor was examined.

Results

Among 38 subjects, 14 patients were male. The age at onset of diabetes was 6.7 ± 3.6 years (range 0.4-14.1). At first abnormal UAE detection, age was 15.3 ± 2.8 years (10.3 - 21.5) and duration of diabetes was 8.7±3.7 years (2.2-16.1). Two patients were prepubertal, and 33 patients were pubertal.

Table 1. Characteristics of the patients in 3 groups and related factors of progression to macroalbuminuria, *P < 0.025, vs. Regress; †P < 0.001, vs. Regress

Microalbuminuria (MicA)		Regress (N = 12)	Persist (N = 15)	Progress (N = 11)
Before micA	Age at onset of DM (years)	9.3±3.1	4.8±3.1*	6.5±3.0
	Pre-HbA1c mean (%)	8.3±1.6	9.3±2.5	12.9±3.3*
	Pre-HbA1c variability (%)	0.6 ±0.9	0.8 ±0.7	1.3 ±1.6
At diagnosis of micA	Age (years)	14.9±2.8	14.2±2.2	17.6±2.4
	Blood pressure (>90p, systolic), n (%)	1 (8%)	3 (21%)	2 (29%)
	Uric acid (mg/dL)	3.6±1.3	4.4±2.5	4.2±4.0
	Total cholesterol (mg/dL)	185±50	168±32	262±52 *
After micA	F/U duration (years)	7.1±3.7	5.6±3.9	6.4±5.2
	Post-HbA1c mean (%)	8.7 ± 1.2	8.9 ± 1.4	11.5±1.4†
	Post HbA1c Variability (%)	1.0 ± 0.4	1.0 ± 0.6	1.6±0.0.6*

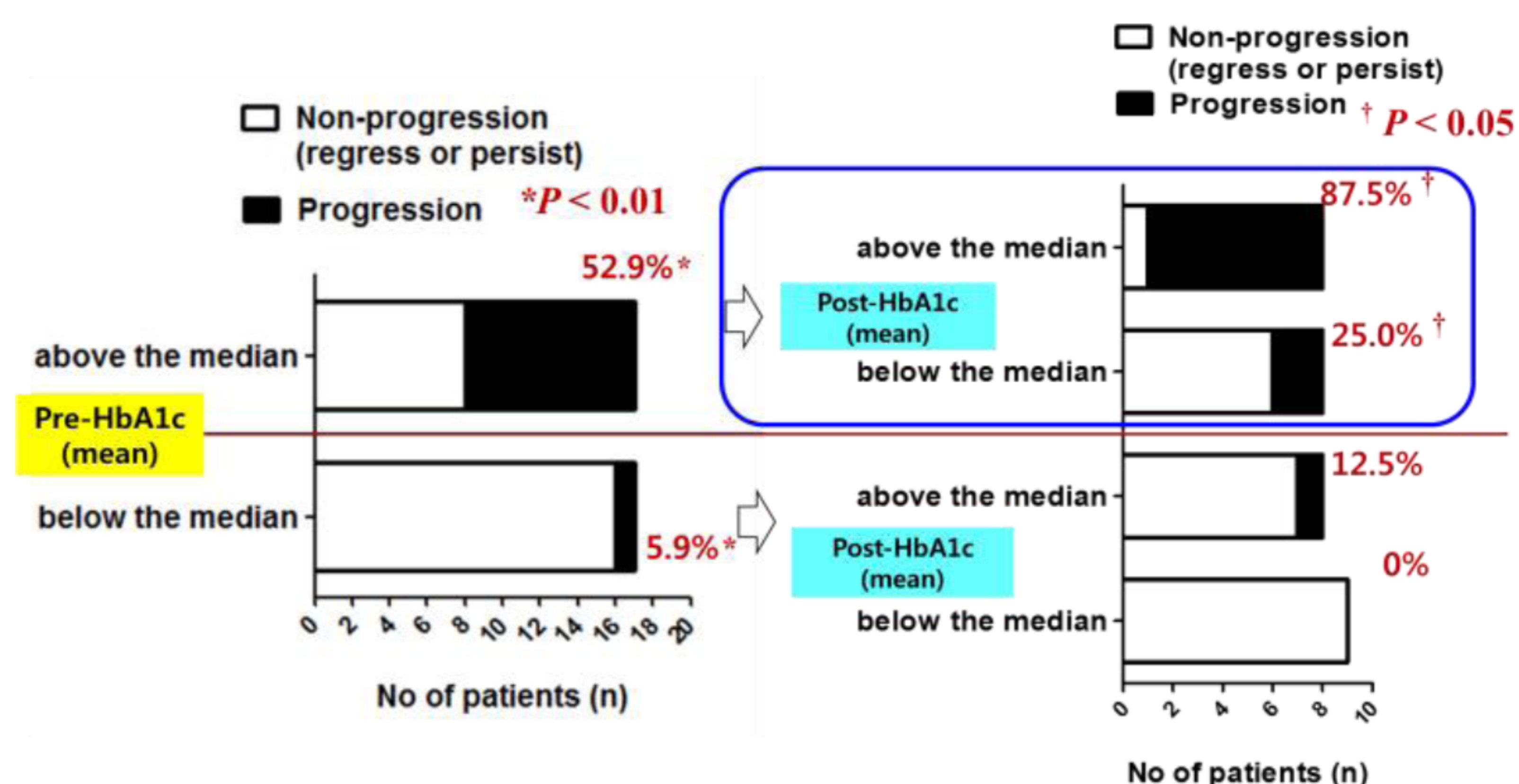Figure 1. The effect of mean HbA1c on progression to macroalbuminuria

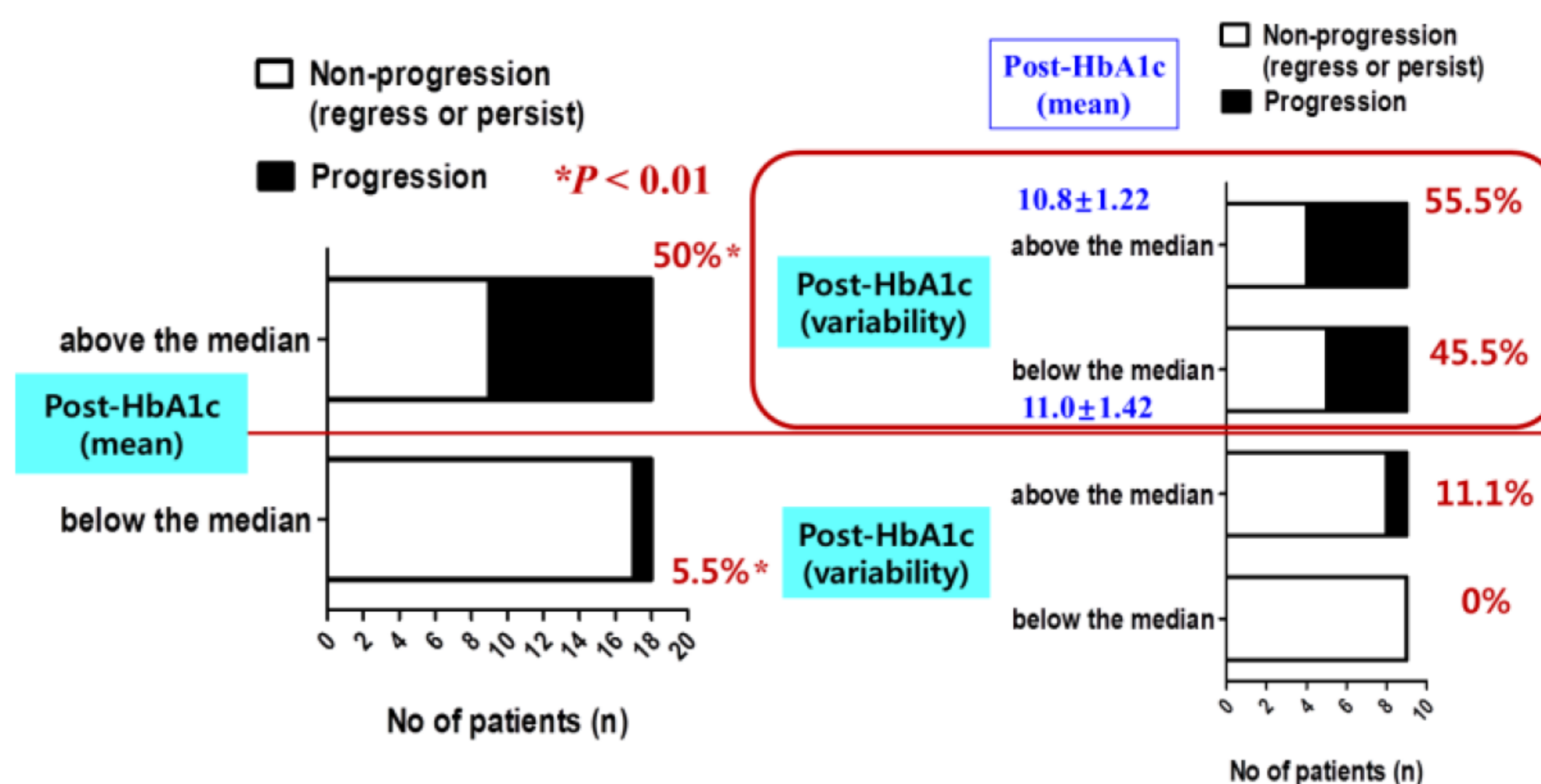Figure 2. The effect of HbA1c variablilty on progression to macroalbuminuria.

Table 2. Cox regression analysis of risk factor for progression to macroalbuminuria.

Univariate analysis			Multivariate analysis		
Variable	HR (95% C.I)	P-value	Variable	HR (95% C.I)	P-value
Pre-A1c (mean)	1.34(1.07-1.70)	0.013	Pre-A1c (mean)	1.52(0.49-4.71)	0.470
Pre-A1c (variability)	3.04(1.10-8.34)	0.031	Pre-A1c (variability)	0.33(0.01-10.2)	0.522
Post-A1c (mean)	14.3(2.73-75.0)	0.002	Post-A1c (mean)	17.9(2.12-151)	0.008
Post-A1c (variability)	2.54(0.99-6.53)	0.053	Post-A1c (variability)	0.22(0.01-9.15)	0.429

Conclusions

Sustained high mean HbA1c was overtly a leading risk factor to progression to macroalbuminuria. Therefore, it is important to maintain a low mean HbA1c. Despite poor glycemic control before diagnosis of microalbuminuria, glycemic control after microalbuminuria may be helpful to prevent progression to macroalbuminuria. Regression to normoalbuminuria was less frequent in patients with longer duration of diabetes at diagnosis of microalbuminuria.

Reference

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