



Impact of smoking habit on survival, glomerulonephritis and its relation to ACE gene I/D polymorphism in hemodialysis patients

Zoltán Kiss¹ | Csaba Ambrus^{2,3} | Lóránt Kerkovits^{2,3} | András Paksy¹ | István Kiss^{2,3,4} | and the BBAVHU-DIALGENE Workgroup²

¹School for Ph.D. Candidates of Aesculap Academy, Budapest

²B. Braun Avitum Hungary (BBAVHU) CPLC Dialysis Network

³Dept. of Nephrology-Hypertension, St Imre University Teaching Hospital, Budapest

⁴Division Section of Geriatrics, 2nd Dept. of Internal Medicine, Semmelweis University Faculty of Medicine, Budapest, Hungary

Background and aim of the study

Previous results suggest that cigarette smoking increases the risk of chronic renal failure particularly in patients with nephrosclerosis and glomerulonephritis. Furthermore, results also give evidences that smoking can promote atherogenesis in renal arteries and it can accelerate the development of end-stage renal disease. In this latter patients group ACE (angiotensin-converting enzyme) gene I/D (insertion/deletion) polymorphism associates survival. The aim of this study was to test the impact of smoking on survival. In addition, we hypothesize that there are associations between smoking habits, glomerulonephritis and ACE gene I/D polymorphism in hemodialysis patients with end-stage renal disease.

Methods

The study design was prospective, observational and multicenter cohort. Data was collected from 716 prevalent chronic hemodialysis patients whose blood samples were genotyped for ACE gene I/D single nucleotide polymorphism. Patients, who were followed up to 144 months, were allocated into groups based on their smoking habits (current smoker, ex-smoker, non smoker), I/D genotype and cause of end-stage renal disease.

Results

Table 1. Baseline characteristics of dialyzed patients by smoking habit (PKD: Polycystic Kidney Disease)

	Smoking habit			Total	P
	I. Current smokers	II. Ex-smokers	I. Non-smokers		
Number of patients % (n)	22.2% (159)	9.8% (70)	67% (480)	100.0% (709)	-
Age, mean±SD (years)	48.1±14.9	58.5±12.9	56.6±15.4	54.9±15.5	I vs II and I vs III, P<0.001
Male % (n)	71.7 (114)	84.3 (59)	42.3 (203)	53.2 (381)	I vs II, P=0.04; I vs III and II vs III, P<0.001
Female % (n)	28.3 (45)	15.7 (11)	57.7 (277)	46.8 (335)	
Cause of ESRD % (n)					
Glomerulonephritis	41.5 (66)	34.3 (24)	24.0 (115)	28.9 (207)	I vs III, P<0.001
Tubulointerstitial	19.5 (31)	15.7 (11)	27.1 (130)	24.2 (173)	II vs III, P=0.04
Diabetes mellitus	6.9 (11)	18.6 (13)	19.4 (93)	16.5 (118)	I vs II and I vs III, P<0.001
PKD	10.1 (16)	8.6 (6)	7.1 (34)	7.8 (56)	NS
Hypertension	3.8 (6)	4.3 (3)	7.7 (37)	6.6 (47)	NS
Other	18.2 (29)	18.6 (13)	14.8 (71)	16.1 (115)	NS
Dialysis vintage, mean±SD (months)	36.2±34.2	31.6±29.9	33.6±31.7	34.0±32.0	NS
ACE-genotype % (n)					
II	19.5 (31)	20.0 (14)	19.8 (95)	19.7 (141)	
ID	47.8 (76)	44.3 (31)	40.8 (196)	42.6 (305)	NS
DD	32.7 (52)	35.7 (25)	39.4 (189)	37.7 (270)	
Frequency of allele % (n)					
I	43.4 (138)	42.1 (59)	40.2 (386)	41.0 (587)	NS
D	56.6 (180)	57.9 (81)	59.8 (574)	59.0 (845)	

Figure 1. Cox proportional hazard model for survival in dialyzed patients

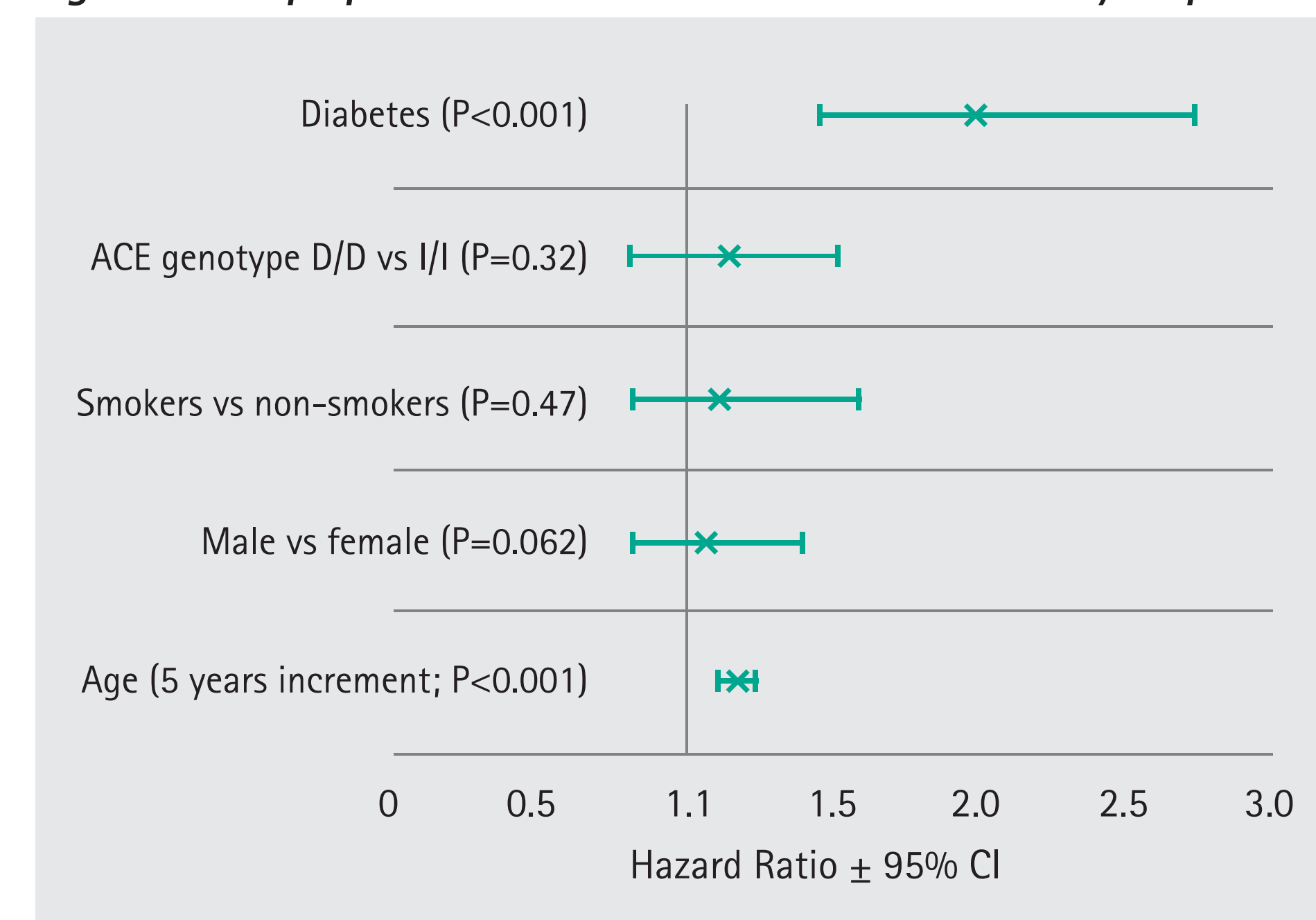


Table 2. Uni- and multivariate logistic regression models with glomerulonephritis as dependent variable

Predictors	Logistic regression					
	OR	95% CI	P	OR	95% CI	P
Age	1.04	1.03-1.06	<0.001	1.04	1.03-1.05	<0.001
Male vs female	2.32	1.66-3.26	<0.001	1.89	1.30-2.73	<0.001
Smoker + ex-smoker vs. Non-smoker	2.05	1.47-2.88	<0.001	1.46	1.01-2.12	0.04
ACE genotype (I/I vs D/D)	1.13	0.73-1.76	0.59	-	-	-

Figure 2. Kaplan-Meier survival estimates for patients with different smoking habits (log-rank test: P=0.15)

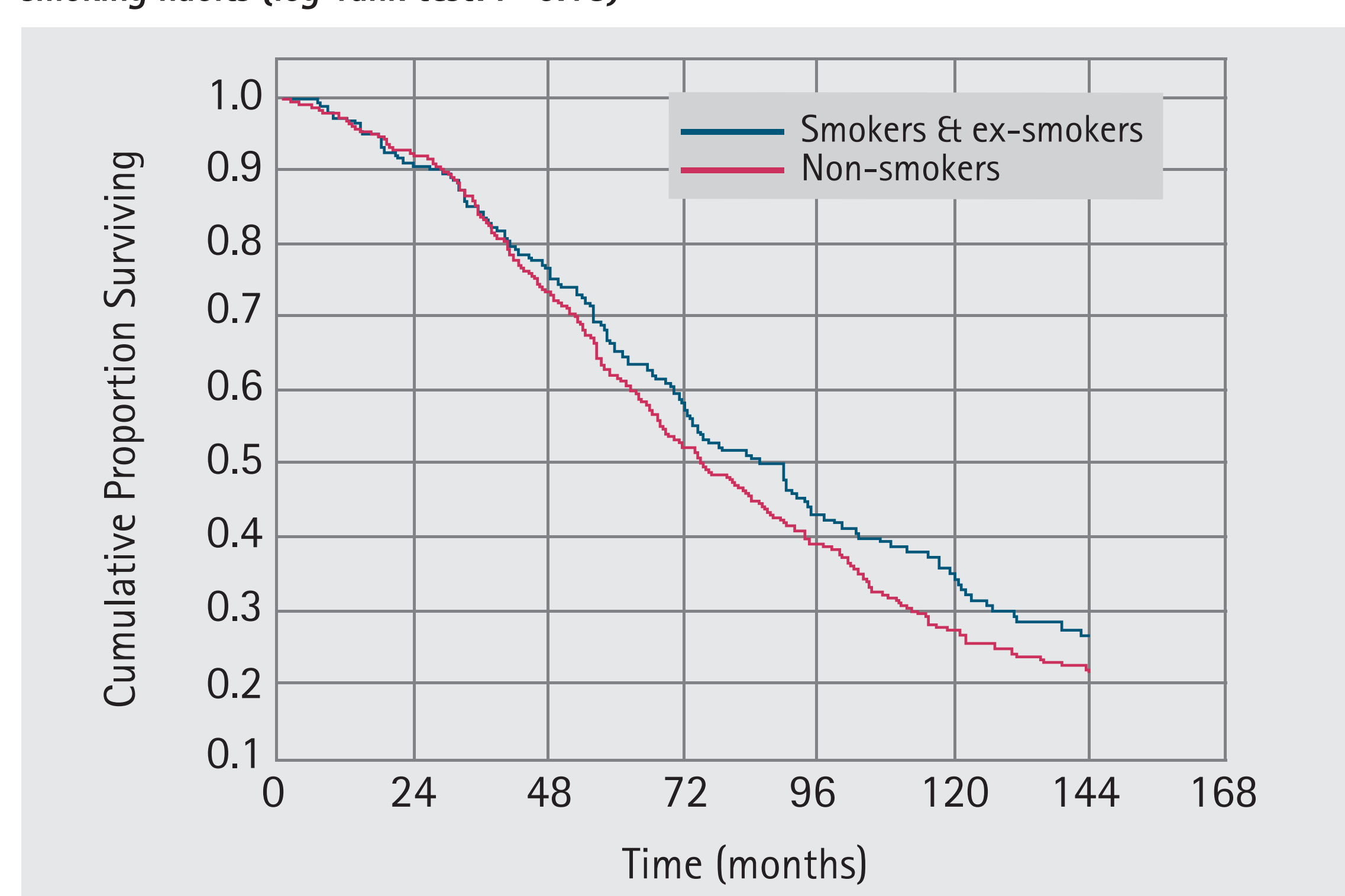
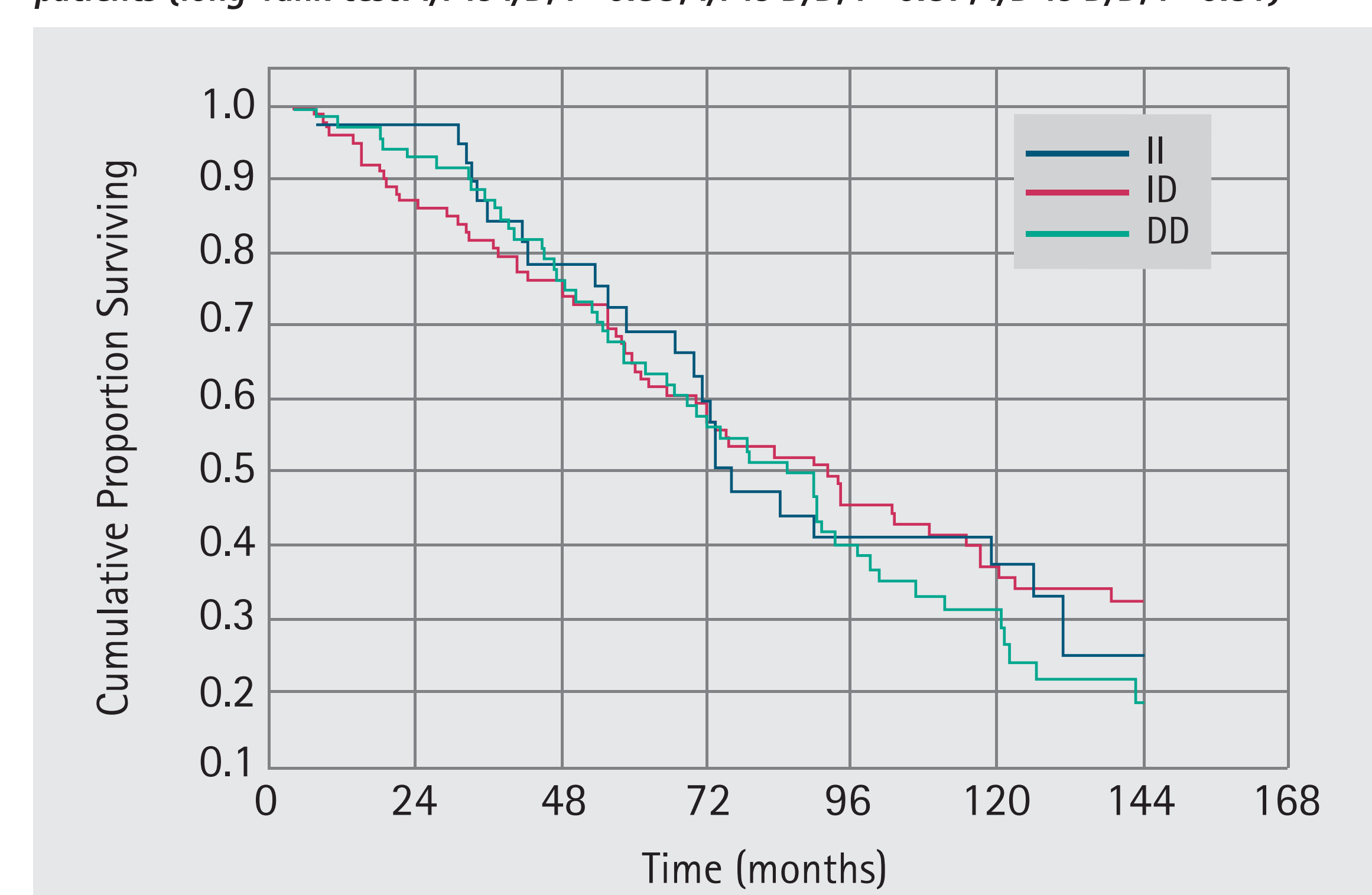


Figure 3. Kaplan-Meier survival estimates for different genotype of smokers and ex-smokers patients (long-rank test: I/I vs I/D, P=0.88; I/I vs D/D, P=0.57; I/D vs D/D, P=0.31)



References & Acknowledgements

- (1) Ejerblad E, Forel CM, Lindblad P et al. Association between Smoking and Chronic Renal Failure in a Nationwide Population-Based Case-Control Study. *J Am Soc Nephrol* 2004;15:2178-2185, (2) Orth SR. Cigarette smoking: an important renal risk factor - far beyond carcinogenesis. *Tobacco Induced Diseases* 2002;1(2):137-155
- The determination of the ACE gene polymorphism was funded by the Hungarian Scientific Research Fund (OTKA,T023927/1997).
- BBAVHU-DIALGENE Workgroup: Attila Benke, Béla Borbás, Sándor Ferenczi, Mária Hengsperger, Szilvia Kazup, Lajos Nagy, József Németh, Antal Rozinka, Tamás Szabó, Tamás Szelestei, Eszter Tóth, Gábor Varga, Gyula Wágner, Gábor Zakar

Conclusions

Our data suggests that smoking has no impact on survival in hemodialyzed chronic kidney disease patients. Furthermore, in this patient group smoking significantly associates with glomerulonephritis while ACE gene I/D polymorphism do not seem to be associated with it. Further research need to clarify the role of smoking in the pathomechanism of glomerulonephritis and also in survival of hemodialysis patients.