NT-proBNP as a significant predictor of cerebrovascular, infectious disease, and tumor death in hemodialysis patients

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OBJECTIVES

As NT-proBNP is a marker of volume overload and myocardial injury, it has been reported as a survival predictor for dialysis patients in terms of all-cause death and cerebrovascular death (CVD) in a relatively small number of patients.

METHODS

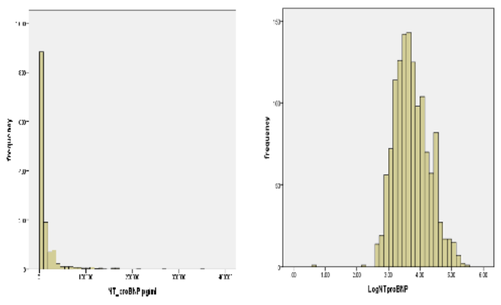
We conducted a prospective cohort study of 1310 patients (41.5% women, 58.5% men) on chronic hemodialysis. Mean age was 67.9 years, mean dialysis vintage was 112 months, and 23.7% of diabetes as a basal kidney disease. A 24-month follow-up was performed.

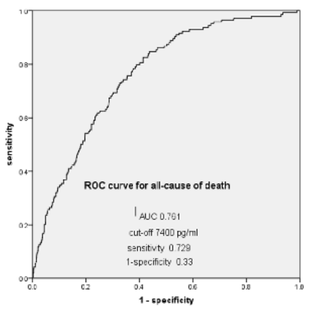
	BNP	NT_proBNP
configuration	BNP	N-fragment
Mr weight	3500	8500
activity	present	none
half period	20 min.	120 min.
metabolic process	NEP、kidney	kidney
sample	plasma	plasma, serum

RESULTS

A total of 144 deaths occurred during the observational period: **53 patients by CVD**, **33 by infectious disease death**, **19 by tumor death**, and 39 by other causes, including those of unknown origin. ROC curve represented 0.761 of AUC and **7400 pg/ml** of NT-proBNP as a cut-off point for predicting all-cause death. Other AUC for CVD, infectious disease death, and tumor death were 0.750, 0.729, and 0.647, respectively. Two groups divided at 7400 pg/ml of NT-proBNP showed clearly distinct survival curve analyzed by Kaplan-Meier methods for all-cause death, CVD, infectious disease death, and tumor death. Cox regression analysis showed NT-proBNP was a significant survival predictor for every endpoint. Hazard ratio (95% CI) was 4.360 (2.892-6.574) for all-cause death, 4.116 (2.054-8.251) for CVD, 2.961 (1.215-7.217) for infectious disease death, and 3.662 (1.230-10.904) for tumor death, adjusted by age, gender, dialysis vintage, cardiothoracic ratio on X-ray, pre-dialysis systolic blood pressure, mean body weight gain from dry weight, and basal kidney disease.

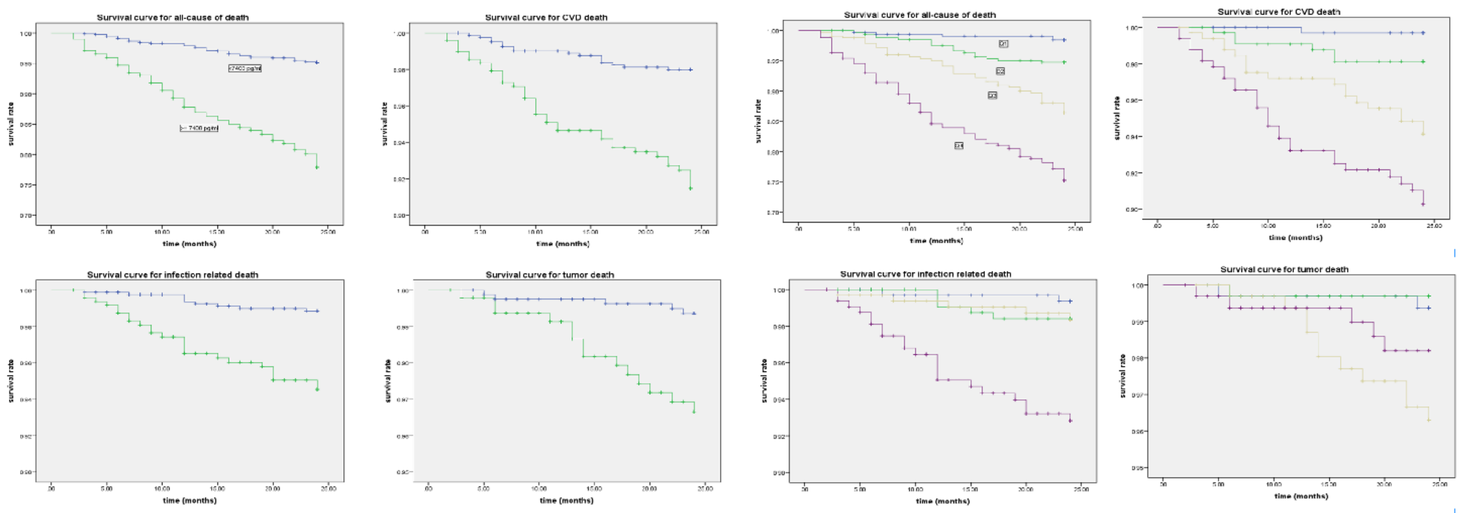
Histogram of NT_proBNP





Cause of death		n
CVD death		
	CHF	29
	AMI	9
	brain hemorrhage	8
	brain infarction	5
	rupture of aortic aneurysm	2
Infectious death	pneumonia	21
	sepsis	10
	others	2
Tumor death	lung cancer	5
	gastric cancer	3
	colon cancer	3
	others	9
Others	sudden death	9
	GI bleeding	2
	others, unknown	27
Total		144

Survival curves (Kaplan-Meier analysis, Log-rank test)



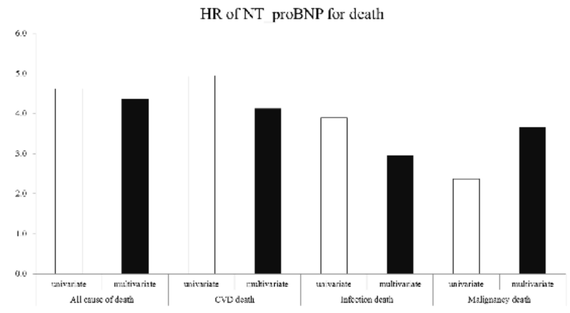
Patients characteristics according to NT_proBNP value

	NT_proBNP<7400 pg/ml	NT_proBNP≥7400 pg/ml	total	p-value
n	820	490	1310	
NT_proBNP	3080 (1812)	29340 (34709)	12903 (24772)	<0.001
LogNTproBNP	3.40 (0.31)	4.30 (0.33)	3.74 (0.54)	<0.001
Age	65.6 (12.7)	71.6 (11.4)	67.9 (12.5)	<0.001
Gender, F(%)	41.3%	41.6%	41.5%	0.954
HD vintage (m)	110 (89)	117 (88)	112 (89)	.1860
CTR (%)	49.9 (4.5)	54.7 (5.4)	51.8 (5.4)	<0.001
pre-HD SBP	153 (19)	158 (22)	155 (20)	<0.001
Dry weight (kg)	54.6 (11.1)	50.1 (10.3)	52.9 (11.0)	<0.001
mean BW gain (%)	4.5 (1.6)	5.0 (2.1)	4.7 (1.8)	<0.001
Basal kidney disease				<0.001
diabetes	21.0%	28.4%	23.7%	
CGN	46.5%	35.9%	42.5%	
nephrosclerosis	11.2%	18.6%	14.0%	
PCKD	5.5%	2.9%	4.5%	
others, unknown	15.9%	14.3%	15.3%	
Causes of death,n				<0.001
CVD	15	38	53	
malignancy	5	14	19	
infection	9	24	33	
others,unknown	10	29	39	

Cox regression analysis (univarate, multivariate)

			HR	95%C.I. lower limit	95%C.I. upper limit
All cause of death	univariate analysis	LogNTproBNP, +1	4.621	3.476	6.142
	multivariate analysis	LogNTproBNP, +1	4.360	2.892	6.574
		Age, +1 y	1.058	1.036	1.080
		Gender, men vs. women	1.211	.810	1.808
		HD vintage, +1 m	.998	.996	1.001
		CTR, +1%	1.012	.970	1.056
		pre-HD SBP, +1 mmHg	.987	.979	.996
		mean BW gain, +1%	.925	.838	1.022
		Basal kidney disease, DM vs. others	1.314	.856	2.018
CVD death	univariate analysis	LogNTproBNP, +1	4.950	3.107	7.886
	multivariate analysis	LogNTproBNP, +1	4.116	2.054	8.251
		Age, +1 y	1.052	1.017	1.088
		Gender, men vs. women	1.192	.621	2.288
		HD vintage, +1 m	1.001	.997	1.005
		CTR, +1%	1.035	.965	1.111
		pre-HD SBP, +1 mmHg	.981	.967	.995
		mean BW gain, +1%	.927	.790	1.089
		Basal kidney disease, DM vs. others	1.198	.572	2.511
Infection death	univariate analysis	LogNTproBNP, +1	3.898	2.150	7.069
	multivariate analysis	LogNTproBNP, +1	2.961	1.215	7.217
		Age, +1 y	1.080	1.030	1.133
		Gender, men vs. women	2.171	.861	5.473
		HD vintage, +1 m	1.001	.996	1.007
		CTR, +1%	1.055	.959	1.161
		pre-HD SBP, +1 mmHg	.992	.974	1.012
		mean BW gain, +1%	.732	.587	.911
		Basal kidney disease, DM vs. others	1.655	.633	4.328
Malignancy death	univariate analysis	LogNTproBNP, +1	2.375	1.067	5.283
	multivariate analysis	LogNTproBNP, +1	3.662	1.230	10.904
		Age, +1 y	1.061	1.003	1.123
		Gender, men vs. women	.908	.285	2.892
		HD vintage, +1 m	.988	.976	1.001
		CTR, +1%	.905	.800	1.025
		pre-HD SBP, +1 mmHg	.997	.970	1.024
		mean BW gain, +1%	.859	.637	1.158

HR of NT_proBNP for death



CONCLUSIONS

NT-proBNP is a strong survival predictor for all-cause death and CVD, and a modest but significant predictor for infectious disease death and tumor death.

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n=109
total death predictor

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n=753
total death & CVD death predictor

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