

# PARATHYROIDECTOMY IMPROVES SURVIVAL IN MATCHED GROUPS

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## OBJECTIVES

To compare outcomes of parathyroidectomy (PTX) with conservative treatment (CT) in matched groups of dialysis patients.

## METHODS

In prospective study in eight dialysis unit in St.-Petersburg from 2009 to 2014 (834 patients) we compared the survival of **84** dialysis patients who received **PTX** in this period with **105** patients on **CT** matched by age, dialysis vintage, PTH levels and phosphatemia (selected from 122 patient who reached **PTH level of 800 pg/ml in repeated tests with calciemia higher 2,5 mmol/l or PTH level of 1000 pg/ml in repeated tests regardless of calciemia** – that could be the indication for PTX – but continued to receive available CT). The study start date for patients in CT was the date of first PTH test later than 6 months after the increase in PTH over indicated levels.

## RESULTS

### Baseline Data

In PTX group gender and age were similar to CT group. Dialysis vintage was slightly higher in PTX group. The baseline PTH median were similar in PTX and CT groups as well as median mean values for previous year. Serum calcium levels were higher by 0.09 mmol/l in PTX group. The phosphate levels were comparable.

### Demography and laboratory data at baseline

	105 pts in Control		84 pts with PTX		p
	Mean	SD	Mean	SD	
Sex, man%	42% (44)		52% (44)		
Age, years	51,8	14,3	48,1	13,7	0,09
Dialysis vintage, m	90,6	68,8	112,6	66,4	0,03
PTH, pg/ml	1181	321	1252	546	0,34
PTH mid-annual, pg/ml	1036	361	1152	523	0,12
Ca, mmol/l	2,38	0,32	2,47	0,24	0,04
Ca midyear, mmol/l	2,4	0,16	2,48	0,2	0,008
P, mmol/l	2,33	0,64	2,51	0,6	0,08
P midyear, mmol/l	2,37	0,57	2,47	0,49	0,25

### Medical treatment (shares)

	Control		PTX		p
	N	%	N	%	
Calcii carbonatis	57	54%	41	49%	0,511
Sevelamer	9	9%	4	5%	0,184
Alphacalcidol	50	48%	39	47%	0,158
Paricalcitol	15	14%	10	12%	0,383
Cinacalcet	35	33%	9	11%	0,00
Almagel	7	7%	3	4%	0,447

### Medical treatment (doses)

	Control		PTX		p
	mean	SD	mean	SD	
Calcii carbonatis, mg/day	1558	904	1250	347	0,091
Sevelamer, mg/day	3489	1833	3556	1794	0,939
Alphacalcidol, µg/day	2,81	1,55	2,36	0,62	0,18
Paricalcitol, µg/day	14,13	5,25	6,25	0,50	0,015
Cinacalcet, µg/day	47,14	16,04	37,50	13,89	0,234

### Overall comorbidity

	Control		PTX		p
	mean	SD	mean	SD	
Comorbidity index (Charlson)	4,96	2,25	4,31	2,04	0,067

### Comorbidity by nosology

	Control		PTX		p
	N	%	N	%	
AMI	14	13%	5	5%	0,10
Congestive heart failure	68	65%	74	70%	0,00
Periferal artery disease	15	14%	12	11%	0,97
Chronic nonspecific pulmonary diseases	14	13%	6	6%	0,18
Peptic ulcer	17	16%	15	14%	0,73
Hepatitis	26	25%	23	22%	0,69
Stroke	16	15%	13	12%	0,40
DM	14	13%	5	5%	0,10
Oncological diseases in history	5	5%	1	1%	0,12

### Laboratory data changes (in one month, mid-annual)

Marked reduction of PTH, Ca and P level were observed In PTX group at the next regular test after study start as well as in comparison of mid-annual values before and after intervention.

In the conservative treatment group significant reduction occurred only for mid-annual phosphate values, and there was a tendency of growing up of mid-annual PTH values.

#### In control group

	Before	After	Difference	95% CI	P
PTH 1 month, pg/ml	1171 ± 319	1143 ± 387	28 ± 356	-45 ± 101	0,449
PTH mid-annual, pg/ml	1040 ± 358	1120 ± 407	-80 ± 471	-174 ± 14	0,094
Ca 1 month, mmol/l	2,37 ± 0,32	2,36 ± 0,27	0,005 ± 0,42	-0,08 0,09	0,908
Ca mid-annual, mmol/l	2,34 ± 0,16	2,38 ± 0,17	0,017 ± 0,15	-0,01 0,05	0,266
P 1 month, mmol/l	2,31 ± 0,64	2,22 ± 0,54	0,09 ± 0,51	-0,01 0,19	0,086
P mid-annual, mmol/l	2,36 ± 0,56	2,24 ± 0,47	0,12 ± 0,49	0,02 0,22	0,015

#### In PTX group

	Before	After	Difference	95% CI	P
PTH 1 month, pg/ml	1250 ± 556	175 ± 195	1075 ± 548	931 ± 1218	< 0,001
PTH mid-annual, pg/ml	1166 ± 527	199 ± 207	966 ± 520	831 ± 1102	< 0,001
Ca 1 month, mmol/l	2,48 ± 0,24	2,13 ± 0,38	0,35 ± 0,45	0,24 ± 0,47	< 0,001
Ca mid-annual, mmol/l	2,49 ± 0,20	2,18 ± 0,29	0,31 ± 0,35	0,22 ± 0,40	< 0,001
P 1 month, mmol/l	2,51 ± 0,61	1,90 ± 0,71	0,61 ± 0,72	0,42 ± 0,79	< 0,001
P mid-annual, mmol/l	2,46 ± 0,50	1,96 ± 0,58	0,51 ± 0,53	0,37 ± 0,64	< 0,001

## Survival

The patient survival since study start was significantly higher in PTX group than in matched CT group (Kaplan-Meier,  $\chi^2=6.78$ ; log-rank-test;  $p=0.009$ ); three- and five-year survival since the study start were 95.4±2.6 v. 80.4±4.8% and 93.0±3.5% v.56.4±8.0% ( $p<0.01$ ).

In adjusted Cox model PTX decreased mortality risk by 63% (95%CI 0+87%;  $p=0.05$ ). Age (+4% per year,  $p=0.008$ ) and phosphatemia level (-7% per 0.1 mmol/l;  $p=0.03$ ) were significant covariates in adjusted model.

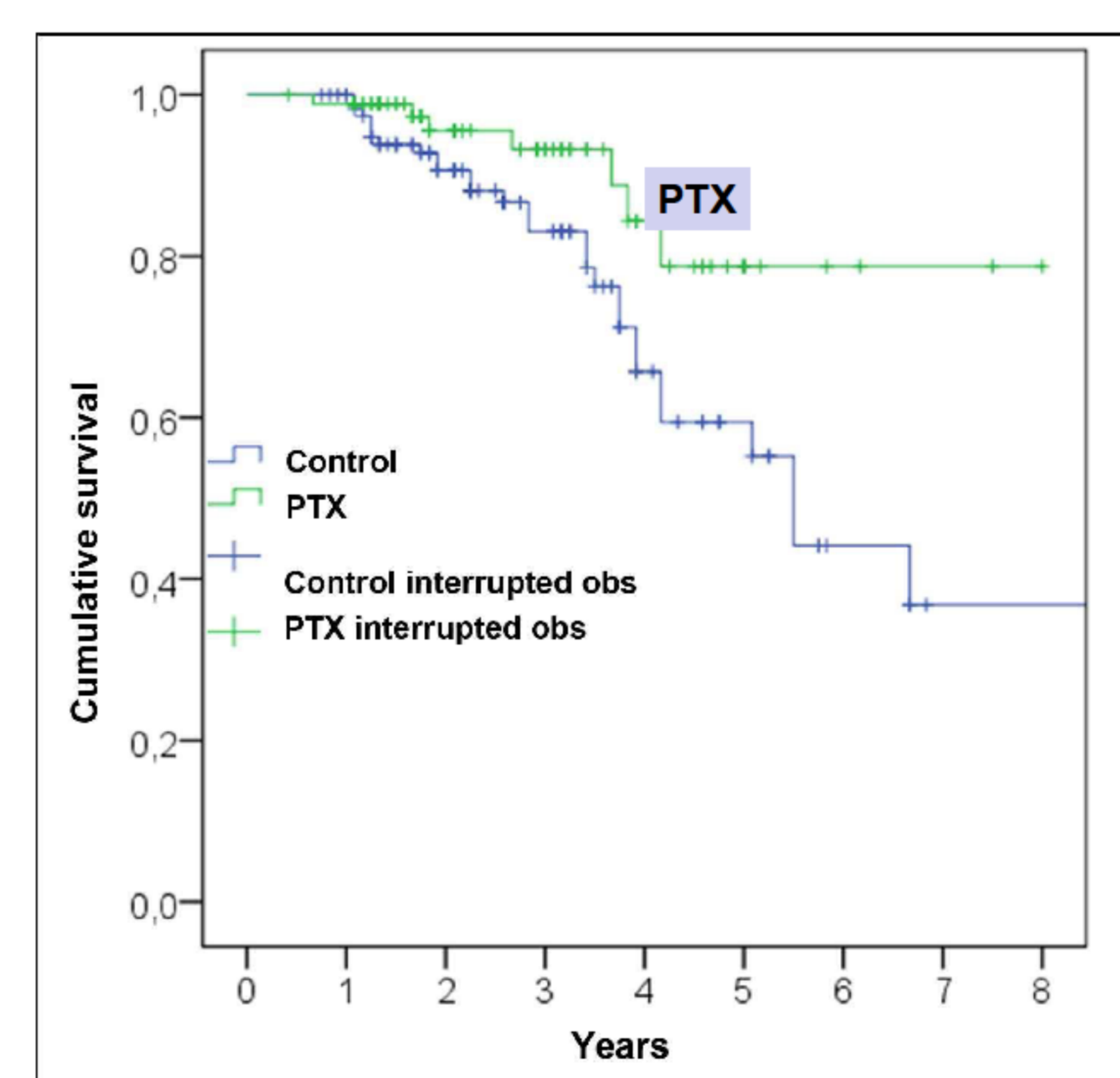
We hypothesized that lower percentage of RRT after study start could be surrogate marker of the early intervention. The Relative Risk of death (RR) reduction in multivariate model was 63% (95%CI 43%+76%) per 10% reduction in percentage of RRT after study start. The RR increased by 2.9% (95%CI 1,3%+4,6%) per month of RRT before study start. The RR reduction for PTX was 73% in this model. The baseline levels of Ca, P, PTH and age were included in the model as covariates. Thus, absolute and relative measure of early intervention were linked with better survival.

### Impact of absolute and relative time to PTX on survival in Cox model

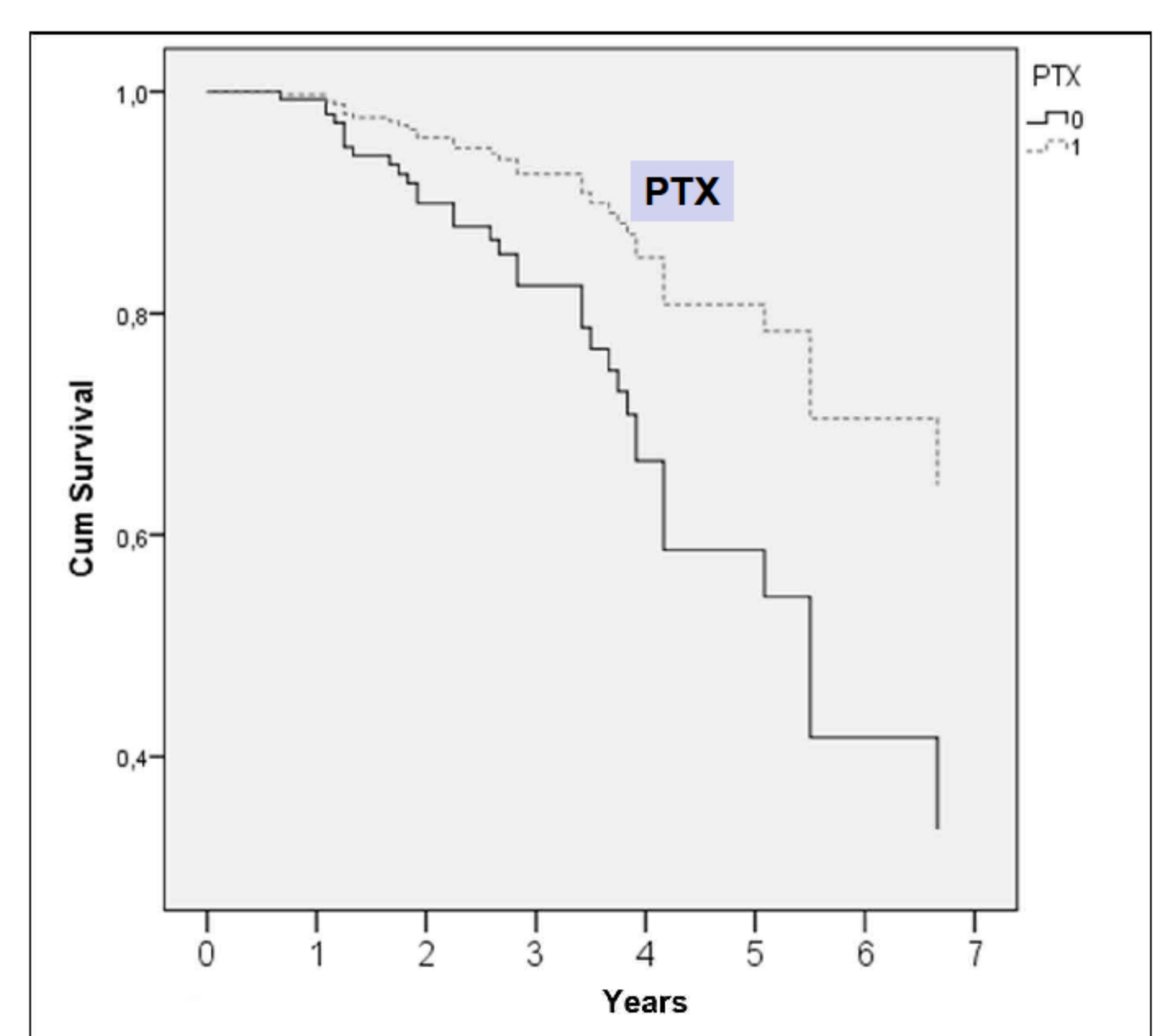
Included factors: PTX, age, dialysis vintage before study start, share of RRT after/before study start, baseline levels of Ca, P, PTH,

Step 5		b	SE (b)	Wald	df	p	Exp(B)	95,0% CI for Exp(B)	
								low	high
	PTH (Cat)	-1,315	,466	7,954	1	,005	,268	,108	,670
	RRT before study start (per month)	,029	,008	12,280	1	,000	1,030	1,013	1,047
	percentage of RRT after study start (per 10%)	-1,000	,225	19,714	1	,000	,368	,237	,572

### Survival comparison by Kaplan-Meier



### Survival comparison in Cox model



### Overall Comparisons

	Chi-Square	df	Sig.
Log Rank (Mantel-Cox)	5,54	1	0,019
Breslow (Generalized Wilcoxon)	3,881	1	0,049
Tarone-Ware	4,764	1	0,029

Included factors: PTX, age, sex, dialysis vintage, baseline levels of Ca, P, PTH

Step 5		b	SE (b)	Wald	df	p	Exp(B)	95,0% CI for Exp(B)	
								low	high
	PTH (Cat)	-0,920	0,433	4,511	1	0,034	0,398	0,170	0,931
	Age (per year)	0,024	0,013	3,437	1	0,064	1,024	0,999	1,051
	Ca (per 1 mmol/l)	1,255	0,784	2,560	1	0,110	3,507	0,754	16,309

## CONCLUSIONS

PTX improved survival In dialysis patients with advanced secondary hyperparathyroidism, resistant to available medical treatment. Relatively earlier intervention had greater effect.

