A DECREASE IN INTACT PARATHYROID HORMONE (iPTH) LEVELS IS ASSOCIATED WITH HIGHER MORTALITY

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BACKGROUND:
The mortality of dialysis patients is 10- to 100-fold higher than in the general population. Baseline serum intact parathyroid hormone (iPTH) levels, and more recently, changes in serum iPTH levels (ΔPTH) over time, have been associated to mortality in dialysis.

METHODS:
We explored the relationship between ΔPTH over 1 year with mortality over the next year in a prospective cohort of 145 prevalent haemodialysis patients from a single center that had median iPTH levels within guideline recommended levels at baseline.

RESULTS:
Median baseline iPTH levels were 205 (116.5, 386.1) pg/ml. Median ΔiPTH between baseline and 1 year calculated in 115 patients was 85.2 ± 57.1 pg/ml. During the second year of follow-up, 27 patients died. ΔiPTH was significantly higher in patients who survived (+157.30 ± 25.82 pg/ml) than in those who died (+39.03 ± 60.95 pg/ml), while baseline iPTH values were not significantly different. The highest mortality (48%) corresponded to patients with a decrease in ΔiPTH (ΔiPTH quartile 1, negative ΔiPTH) and the lowest (12%) to quartile 3 (ΔiPTH increase 101-300 pg/ml). In a logistic regression model, ΔiPTH was associated with mortality with an odds ratio (OR) of 0.998 (95% CI 0.996-0999, p=0.038). In multivariable analysis, mortality risk was 73% and 88% lower for patients with ΔiPTH 0-100 pg/ml and 101-300 pg/ml than for those with a decrease in ΔiPTH. The OR for death of a decrease in ΔiPTH was 4.131 (1.515-11.27) (p=0.006).

Variable	OR (95% CI)	P value
Baseline age (years)	1.062 (1.030 – 1.096)	**< 0.01**
Female sex	0.607 (0.301 – 1.225)	0.162
Dyalisis vintage (years)	1.009 (0.942 – 1.080)	0.806
Baseline PTH (pg/ml)	1.001 (1.000– 1.002)	0.071
Baseline FGF23 (RU/ml)	1.000 (1.000 – 1.000)	0.327
Baseline calcium (mg/dl)	1.260 (0.792 – 2.002)	0.328
Baseline phosphate (mg/dl)	0.974 (0.888 – 1.068)	0.424
Baseline 25 (OH) Vit D (ng/dl)	0.996 (0.987 – 1.000)	0.321
Baseline albumin (g/dl)	0.379 (0.171 – 0.843)	0.013
ΔiPTH (pg/ml)		
Q1 < 0	3.815 (1.452 – 10.03)	**0.007**
Q2 0-100	0.735 (0.260 – 2.074)	0.555
Q3 101 – 300	0.120 (0.029 – 0.502)	**0.004**
Q4 > 300	0.464 (0.135 – 1.600)	0.224

Univariate logistic regression models for predicting mortality. Higher baseline age, lower baseline serum albumin and a decreasing ΔiPTH (ΔiPTH <0 pg/ml) within the first year are predictors of mortality.

Variable	OR (95% CI)	P value
Age (years)	1.039 (1.001 – 1.079)	**0.044**
ΔiPTH (pg/ml)		
0 – 100	0.265 (0.076 – 0.924)	**0.037**
101 – 300	0.115 (0.027 – 0.490)	**0.003**
> 300	0.469 (0.130 – 1.690)	0.247

Multivariable regression model for mortality prediction considering quartiles of ΔiPTH within the first year. Q1 ΔiPTH (ΔiPTH <0 pg/ml) was the comparator.
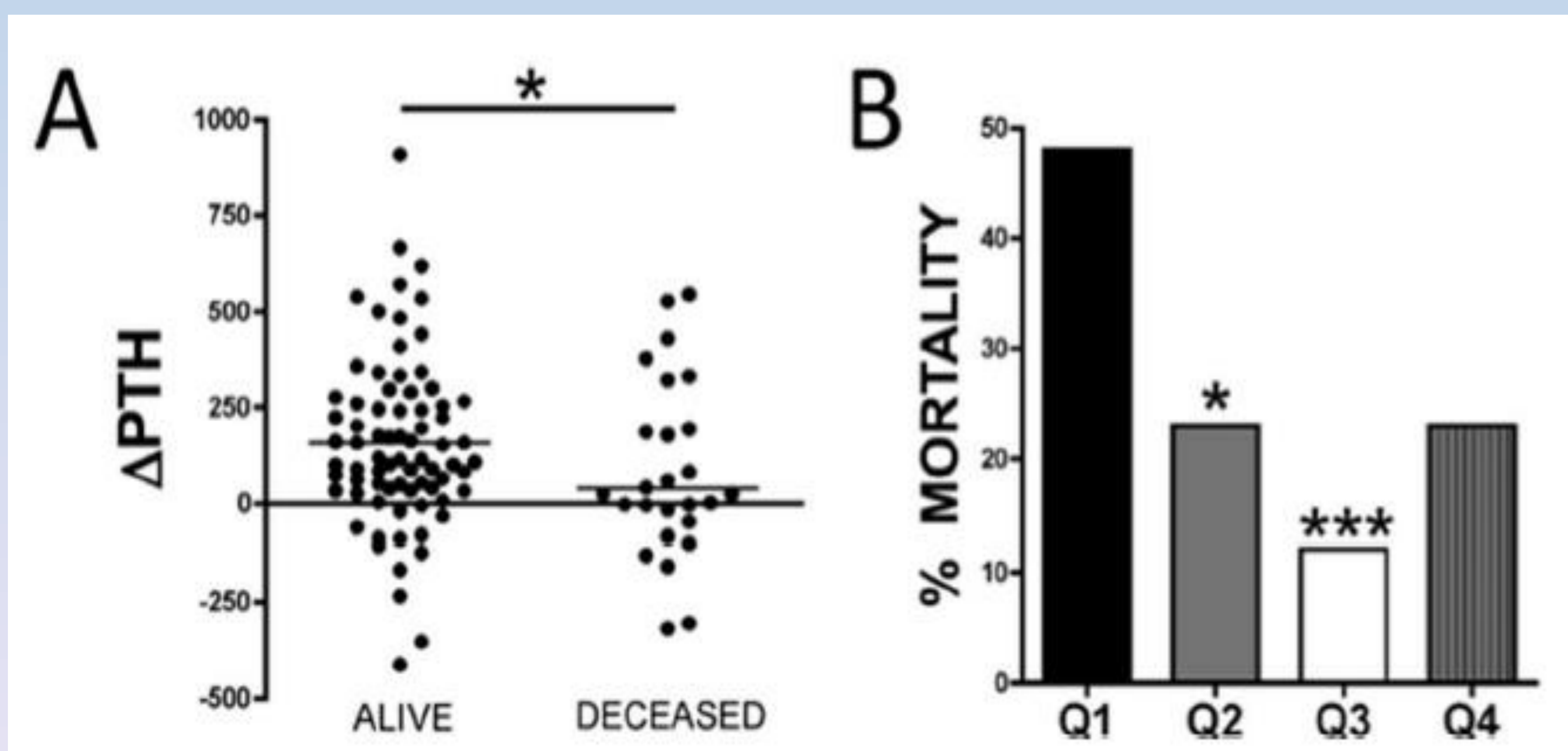
Changes in iPTH (ΔiPTH,pg/ml) during the first 12 months and mortality at 24 months.
(A) Comparison of ΔiPTH within the first 12 months between survivors and deceased patients at 24 months. The mean ΔiPTH was higher in survivors than in deceased patients. * *P <0.05.*
(B) *Graphic representation of* mortality according to quartiles of ΔiPTH in the first year: Q1 ΔiPTH <0 pg/ml; Q2 0±100 pg/ml; Q3 101±300 pg/ml; Q4 >301 pg/ml. * *P <0.05* *** p <0.001 vs Q1.*

CONCLUSIONS:
In prevalent hemodialysis patients with median baseline iPTH values within the guideline recommended range, a decrease in ΔiPTH was associated with higher mortality. Further studies are required to understand the mechanisms and therapeutic implications of this observation which challenges current clinical practice.