Impact of serum calcitriol levels on haemodialysis patients' survival rate.

Guillaume JEAN, Christie LORRIAUX, Patrik DELEAVAL, Jean-Marc HUROT, Brice MAYOR, Charles CHAZOT.

NEPHROCARE Tassin-Charcot, Haemodialysis and Nephrology, Sainte Foy-les-lyon, France

OBJECTIVES

Vitamin D deficiency has been associated with poor outcomes in haemodialysis (HD) patients (1), but no data is available on serum calcitriol (1,25D) levels impact on survival rate. Besides, 1,25D could be modified by vitamin D prescription (native and calcitriol/analogs (2).
Aim: To assess the impact of serum 1,25D levels and vitamin D treatments on HD patients 'survival rate.

METHODS

All prevalents HD patients of the centre have been included with baseline 25-hydroxyvitaminD (25D) and 1,25-D values and vitamin D prescription. Patients were dialyzed 3 time weekly (4 to 8-hours) using polysulfone high-flux filters FX 60, 80, 100, 800 and 1000 (Fresenius Medical Care©, Bad Homburg, Germany) in HD or online postdilution haemodiafiltration (HDF). Blood flow rate ranged from 220 to 400 ml/min, dialysate flow rate ranged from 350 to 800 ml/min. The standard dialysis calcium concentration was 1.5 mmol/L, but 1.25 mmol/L was prescribed in cases where the PTH level was low (< 100 pg/mL) while 1.75 mmol/L was recommended in cases where the PTH level was high (> 400 pg/mL). Blood samples were obtained from nonfasting patients before a mid-week dialysis session. All laboratory parameters were measured in the same blood draw. 25-hydroxyvitamin D (25-OHD) analyses were performed using Architect automat 25-D assays (Abbott© Laboratories. Abbott Park, Illinois, U.S.A.): a chemiluminescent microparticle immunoassay. Calcitriol (1,25-OH2D) was measured after extraction by using a radioimmunoassay (LIAISON; DiaSorin© Inc., Stillwater, MN, USA). Survival rate was compared (Kaplan-Meier and Cox model) according to 1,25D quartiles and alfacalcidol prescription (Alfa+ or Alfa-).

RESULTS

	Quartile 1	Quartile 2	Quartile 3	Quartile 4
Age years	66.5 ± 15	68.2 ± 13	67.3 ± 12	65.3 ± 14
Dialysis vintage months	63.8 ± 76	72.6 ± 86	68.3 ± 71	68.8 ± 67
Female gender %	42.6	40.8	47.2	50
Diabetes %	39.3	44.9	39.6	31.5
Cardiac disease %	23	26.5	20.8	14.8
Peripheral vascular disease %	23	20.5	22.6	27.8
Stroke %	11.5	20.4	17	9.2
Chronic liver disease %	18	20.4	15.1	20.4
BMI kg/m²	23.6 ± 5	23.7 ± 4	25 ± 5	26.4 ± 6
Dry body weight kg	63.7 ± 13	63.1 ± 11	70 ± 16	71 ± 16
Native AV fistula %	85	91	92.5	97
Dialysis session time hr : mn	6 : 15 ± 1: 15	6 : 20 ± 1: 15	6 : 30 ± 1 : 4	6 : 35 ± 1 : 38
Dialysate calcium mmol/L	1.46 ± 0.1	1.49 ± 0.08	1.48 ± 0.05	1.49 ± 0.03
Kt/V	2.15 ± 0.6	2.3 ± 0.6	2.4 ± 0.8	2.5 ± 0.8
nPNA g/kg/day	1.24 ± 0.3	1.27 ± 0.3	1.32 ± 0.3	1.25 ± 0.3
PTH pg/mL	240 ± 189	265 ± 177	293 ± 174	305 ± 199
Calcaemia mmol/L	2.25 ± 0.1	2.29 ± 0.1	2.31 ± 0.1	2.35 ± 0.1
Phosphataemia mmol/L	1.37 ± 0.4	1.31 ± 0.3	1.36 ± 0.3	1.33 ± 0.2
B-ALP µg/L	18.1 ± 10	22.6 ± 11	21.5 ± 18	20.5 ± 13
Albumin g/L	33.3 ± 5	35.1 ± 4	34.6 ± 3	36.9 ± 4*
CRP mg/L	16.3 ± 23	8.3 ± 10	8.9 ± 9	16.3 ± 37
1.25-OH2D pmol/L	<4*	15 ± 3	29 ± 4	57 ± 20
25-OHD nmol/L	66.6 ± 26*	71 ± 35	82 ± 39	89 ± 41
CaCO3 % (g/d)	12.4 (1.8±0.8)	10.9 (2±0.7)	5.6 (1.9±0.9)	9.2 (2±0.6)
Sevelamer % (g/d)	23 (3.2±0.9)	24 (3.3±1.6)	31 (3.5±1.6)	29 (3.5±1.5)
Calcidiol % (µg/day)	86 (17±8)	91 (19±9)	94 (18±8)	92 (17 ±6)
Alfacalcidol % (µg/week)	20 (2.2±1.3)	24 (4.6±4)	52 (2.5±1.4)*	92 (2.9±1.6)*
Cinacalcet % (mg/d)	5 (50±17)	8.3 (37±27)	2.4 (50±18)	2.2 (56±34)
Hip T-score	-2.5 ± 1.5	-2.3 ± 1.3	-2 ± 1.3	-1.8 ± 1.2

Table 1: Baseline data according to serum calcitriol quartiles

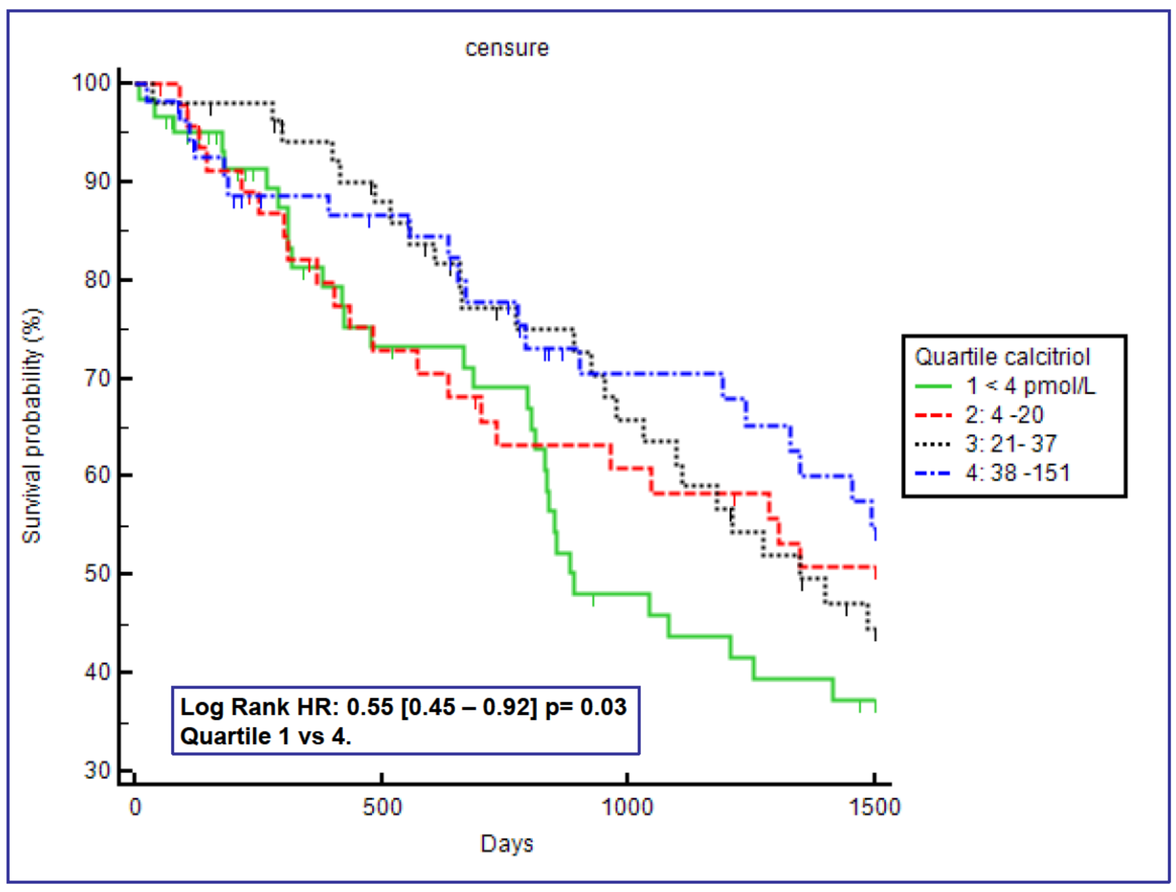

Figure 1: Survival rate (Kaplan-Meier) according to the baseline serum calcitriol quartile

Covariate	b	SE	P	Exp(b)	95% CI of Exp(b)
Quartile =2	-0.6	0.28	0.03	0.54	0.33 to 0.95
Quartile=3	-0.58	0.27	0.04	0.55	0.32 to 0.97
Quartile=4	-0.70	0.33	0.02	0.46	0.24 to 0.87
Age years	0.06	0.011	<0.0001	1.0668	1.04 to 1.09
Dialysis vintage Months	-0.001	0.0014	0.29	0.99	0.99 to 1.001
25OHD nmol/L	-0.001	0.002	0.70	0.99	0.99 to 1.004
Male Gender	0.05494	0.20	0,79	1.05	0.70 to 1.58
Alfacalcidol y/n	0.05	0.25	0.8	1.05	0.64 to 1.7

Table 2: Survival rate (Cox model) according to the baseline serum calcitriol quartile adjusted for age, dialysis vintage, 25OHD and gender.

RESULTS

A total of 222 prevalent HD patients were included in 2005. Baseline data is displayed in Table 1. More than 85% of the patients received calcidiol (25OHD: 18 ± 8 µg/day), dialysis session time ranged from 5 to 8-hrs.
As compared with patients of the 4th quartiles (1,25D-4: 38-151 pmol/L), patients of the 1st quartile (1,25D-1 : < 4 pmol/L) were less frequently Alfa+ (20 vs. 92%, p< 0.001) and have lower 25D serum levels (64.6 ± 26 vs 89 ± 41 nmol/L, p= 0.001).
Patients of the 4th quartile displayed **lower all-causes mortality** rate vs. patients of 1st quartile (Log Rank HR: 0.55 [0.45 – 0.92] p= 0.03, Figure 1) and in Cox model adjusted for age, dialysis vintage, serum 25D level and gender (HR: 0.46 [0.27 – 0.87] p= 0.02), (Table2).
Alfa+ patients displayed lower mortality rate vs. Alfa- (Log Rank: 0.65 [0.43 – 0.9] p=0.03) that was not significant using Cox model. **Alfa + / 1,25D-4 patients displayed lower mortality rate** than did Alfa-/1,25D-1 patients (Log Rank: 0.5 [0.27 – 0.9] p= 0.02) and than did Alfa+/1,25D-1 in Cox (HR: 0.35 [0.11 – 0.98] p=0.05) Figure 2.

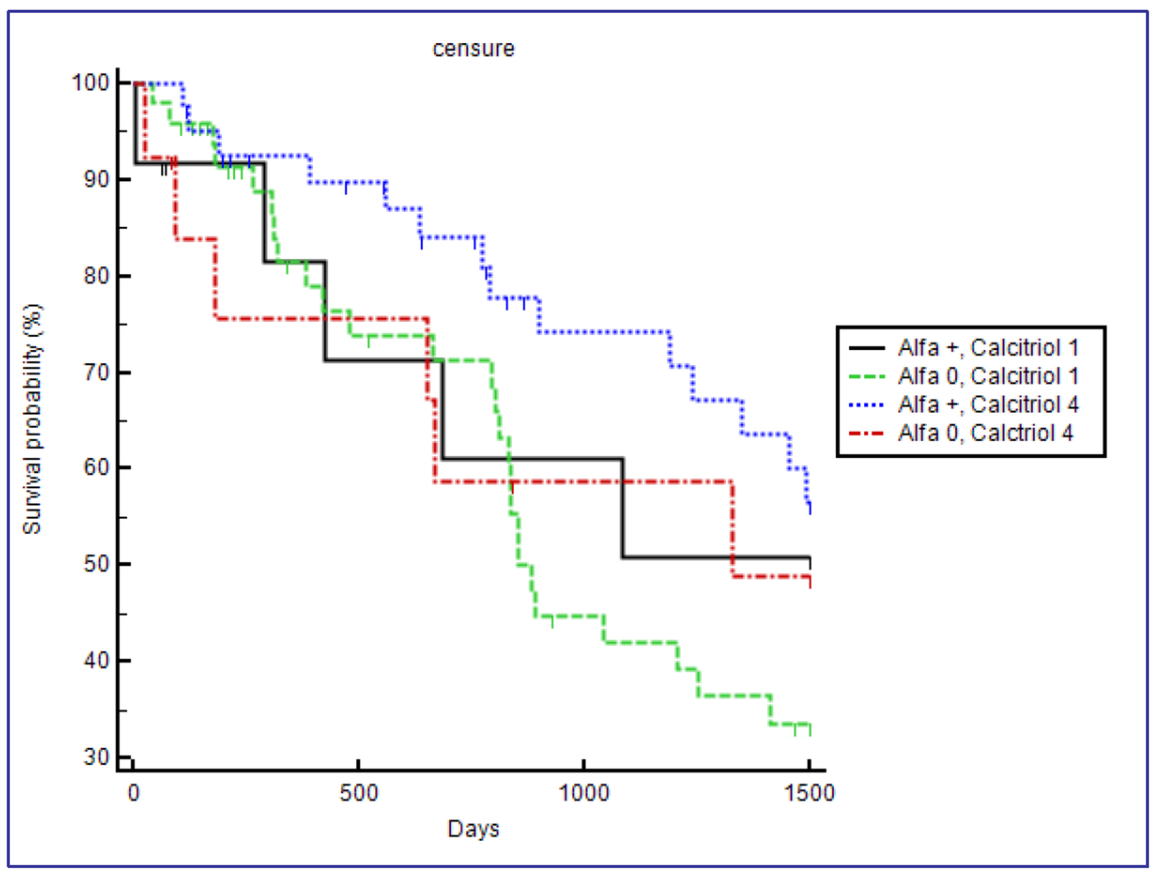

Figure 2: Survival rate (Kaplan-Meier) according to the baseline treatment with alfacalcidol (+ or 0) and calcitriol quartile (1 or 4).

CONCLUSION

This is the first observational study showing higher mortality rate in HD patients with lower serum 1,25D levels despite general 25D supplementation.
Lack of alfacalcidol treatment appears also harmful when 1,25D is low.
This data should be confirmed before recommending 1,25D supplementation in calcitriol deficient patients.

*1) Jean, G.,, et al. (2011). "Impact of hypovitaminosis D and alfacalcidol therapy on survival of hemodialysis patients: results from the French ARNOS study." Nephron Clin Pract **118**(2): c204-210*
*2) Jean, G., et al. (2009). "Monthly cholecalciferol administration in haemodialysis patients: a simple and efficient strategy for vitamin D supplementation." Nephrol. Dial. Transplant. **24**(12): 3799-3805.*

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