Vitamin D prescription is associated with better survival rate: result from the ARNOS study.

Guillaume JEAN 1, Xavier MOREAU-GAUDRY 2 , Denis FOUQUE 3, and all the ARNOS investigators.

1) NEPHROCARE Tassin-Charcot, Haemodialysis and Nephrology, Sainte Foy-les-lyon, France: 2) AGDUC Haemodialysis, Montélimar, France;

3) Centre Hospitalier Lyon-Sud, Nephrology, Dialysis and Nutrition, Pierre Benite, France.

OBJECTIVES

Vitamin D deficiency has been associated with higher mortality rate in CKD (1) and dialysis patients (2). RCT's showing beneficial impact of vitamin D prescription, native or active, on outcomes are lacking. Aim: From the ARNOS (Association Régionale des Néphrologues OStéopathie) French cohort, comparing haemodialysis (HD) patients survival rate according to native (ergo- or cholecalciferol) and active (calcitriol or analogs) vitamin D prescription.

METHODS

The patients were extracted from the ARNOS database, which includes information on 1348 patients followed from July 2005 to January 2009 in 25 dialysis centres in the Rhône-Alpes area.

We examined prospectively collected data of a 42-month cohort of all prevalent HD patients. The ARNOS study contains detailed demographic and clinical data, including comorbidities, laboratory results at baseline and every 6 months thereafter for 42 months. Most blood samples were collected pre-dialysis with the exception of the post-dialysis serum urea, which was obtained in order to calculate urea kinetics. Total serum calcium, phosphorus, albumin, urea, and second generation parathyroid hormone (PTH) (Roche Elecsys©) levels were recorded. The normalized protein nitrogen appearance, also known as the protein catabolic rate (nPCR), and the Kt/V were calculated using urea kinetic modelling formulas (Daugirdas 2nd generation single pool).

We compared the 42-months survival rate of patients according to the initial **prescription of vitamin D: none (NoVD), native (NVD), active (AVD) or their association (NAVD),** using Kaplan-Meier and Cox model.

RESULTS

	No D N= 502	Native D N= 237	Active D N= 391	Both D N= 218
Age years	66.2 ± 13	68.5 ± 15	67.3 ± 13	63.9 ± 15*
Dialysis vintage months	61.2 ± 79	64.2 ± 75	62.5 ± 75	61.1 ± 74
Female gender %	41	40	38	40
Diabetes %	37	27	29	26
Cardiac disease %	28	22	26	17*
Peripheral vascular disease %	41	39	33	30*
Stroke %	9	9.1	13	13.2
Chronic liver disease %	7.5	8.1	9.3	10.6
BMI kg/m²	25.1 ± 4	24 ± 4	25 ± 5	24.7 ± 4
Dry body weight kg	68.7 ± 14	64.8 ± 14	67.7 ± 14	67 ± 14
Native AV fistula %	81	90	81	92
HDF %	17	34*	13	14
Dialysate calcium mmol/L	1.48 ± 0.1	1.51 ± 0.1	1.48 ± 0.1	1.51 ± 0.1
Kt/V	1.37 ± 0.3	1.56 ± 0.4	1.44 ± 0.4	1.66 ± 0.5*
nPNA g/kg/day	1 ± 0.2	1.1 ± 0.3	1 ± 0.2	1.1 ± 0.3
PTH pg/mL	280 ± 306	227 ± 264	278 ± 323	271 ± 238
Calcaemia mmol/L	2.25 ± 0.2	2.29 ± 0.2	2.27 ± 0.2	2.3 ± 0.18
Phosphataemia mmol/L	1.65 ± 0.5	1.58 ± 0.5	1.54 ± 0.5	1.43 ± 0.4
Albumin g/L	36 ± 5	36 ± 5	36.4 ± 4	36.1 ± 5
CRP mg/L	15.1 ± 28	12 ± 17	13.8 ± 27	11 ± 19
25-OHD (ng/L)	11.5 ± 4	38 ± 35	12 ± 4	36 ± 37
CaCO3 % (g/d)	56 (1.8 ± 1.3)	54 (1.3 ± 1)	60 (2 ± 1.2)	47*(1.8 ± 1.3)
Sevelamer % (g/d)	44 (3.8 ± 1.8)	36 (3.5 ± 2.1)	42 (4.1 ± 1.8)	42 (4 ± 2.2)
Native D U/day	0	1003 ± 674	0	1100 ± 375
Alfacalcidol µg/week	0	0	2.6 ± 2	2.8 ± 2.2
Cinacalcet % (mg/d)	7 (51 ± 24)	11 (44 ± 21)	6.7 (45 ± 22)	17*(42 ± 18)

Table 1: Baseline characteristic's.

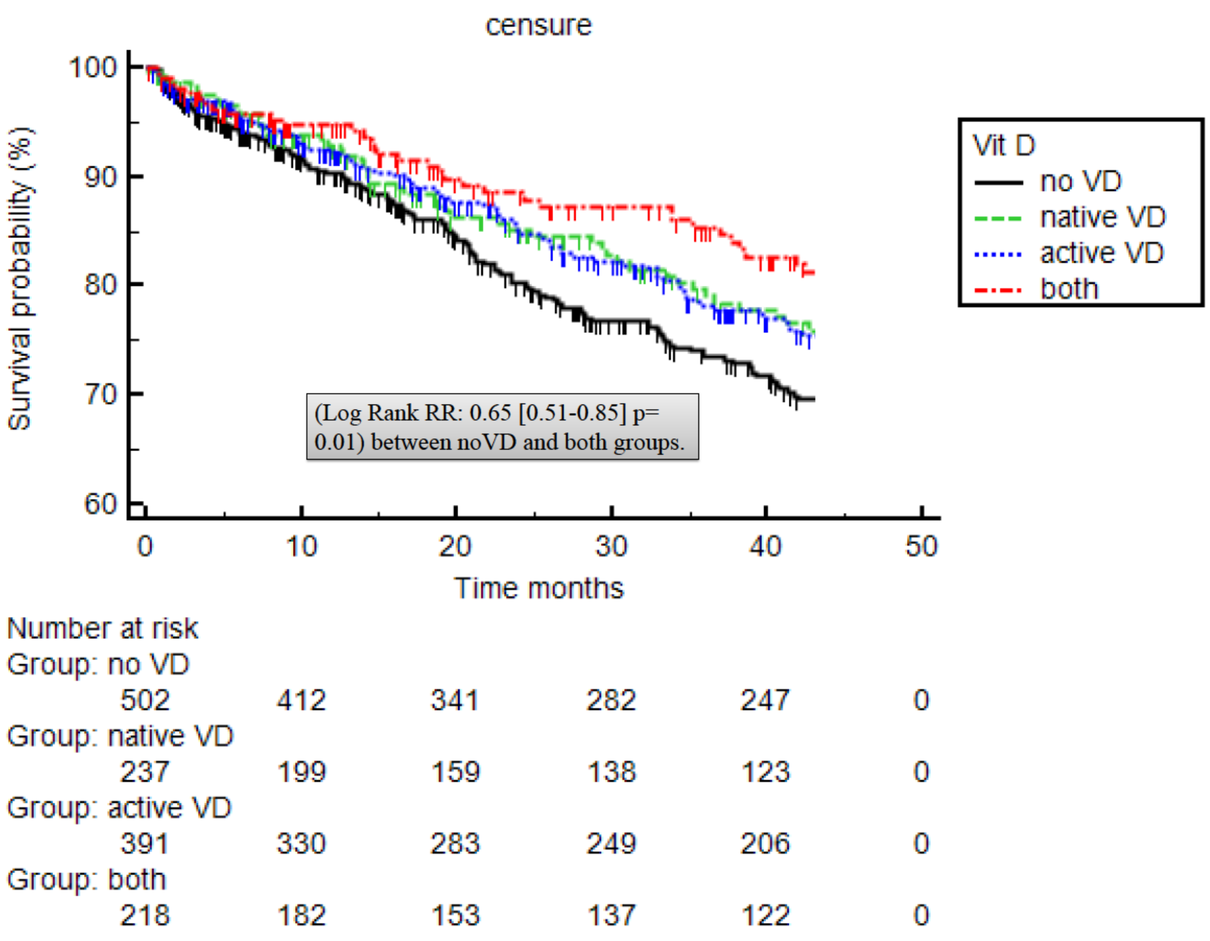

Figure 1: Survival analysis (Kaplan-Meier) according to the vitamin D prescription.

RESULTS

1348 HD patients have been included in 25 centres: 502 were of NoVD group (37.2%), 237 NVD (17.5%), 391 AVD (29%) and 218 NAVD (16.2%). Baseline characteristic's are displayed on Table 1.

NAVD patients were younger, less frequently diabetics with less frequent previous cardiovascular (CV) events. Mean daily native vitamin D dosage was 1000 UI (800 to 6600 UI of ergo-cholecalciferol); alfacalcidol dosage was 2.7 µg/week (1.5 – 7 µg). In univariated analysis, only the NAVD group displayed a survival advantage vs. NoVD (Log Rank RR: 0.65 [0.51-0.85] p= 0.01). According to the Cox model adjusted for age, diabetes, and CV history, this advantage remains significant (HR: 0.69 [0.51-0.97] p= 0.04).

Covariate	b	SE	P	Exp(b)	95% CI of Exp(b)
NVD	-0,1767	0,1267	0,1632	0,8380	0,6545 to 1,0730
AVD	-0,1477	0,1060	0,1636	0,8627	0,7016 to 1,0608
NAVD	**-0,4176**	**0,1409**	**0,04**	**0,698**	**0,512 to 0,969**
Age years	0,03939	0,004020	<0,0001	1,0402	1,0320 to 1,0484
Diabetes y/n	0,2597	0,09258	0,0050	1,2966	1,0824 to 1,5531
CV history y/n	0,3815	0,09421	0,0001	1,4645	1,2187 to 1,7598

Table 2: Survival analysis (Cox Model) comparing the 3 vitamin D groups to the NoVD group .

CONCLUSION

In this observational study, we showed for the first time a survival advantage for HD patients with concomitant prescription of both native and active vitamin D derivates as compared with patient without vitamin D prescription. We have previously reported, in the same cohort, a survival advantage for patient with serum 25-OHD > 18 ng/mL (2). Serum calcitriol value is lacking in ARNOS, but it is hypothesized that it could be associated with outcomes explaining our results.

*1) Ravani, P., et al. (2009). "Vitamin D levels and patient outcome in chronic kidney disease." Kidney Int **75**: 88-95.*

*2) Jean, G.,et al. (2010). "Impact of Hypovitaminosis D and Alfacalcidol Therapy on Survival of Hemodialysis Patients: Results from the French ARNOS Study." Nephron Clin Pract **118**(2): c204-c210.*

The ARNOS study was supported by Amgen Inc France.

DOI: 10.3252/pso.eu.52era.2015

ePosters supported by F. Hoffmann- La Roche Ltd.