# CLINICAL ASPECTS OF VITAMIN D PATHWAY GENE POLYMORPHISMS IN HEMODIALYSIS WOMEN AND MEN

Alicja E. Grzegorzewska 1, Grzegorz Ostromecki 2, Adrianna Mostowska 3, Anna Sowińska 4, Paweł P. Jagodziński 3

- 1. Chair and Department of Nephrology, Transplantology and Internal Diseases, Poznań; University of Medical Sciences (PUMS), Poznań, Poland
- 2. DaVita Clinic Piła Dialysis Center, Piła, Poland
- 3. Chair and Department of Computer Science and Statistics, PUMS, Poznań, Poland
- 4. Chair and Department of Biochemistry and Molecular Biology, PUMS, Poznań, Poland

# Background/Objectives:

Vitamin D is casually associated with life-threatening diseases like myocardial infarction, cerebral stroke, and bone mineral disorders. Prevalence of these diseases is gender-dependent.

### Patient characteristics

Parameter	HD women	HD men	D	
Demographic data	n = 431	n = 625	P value	
Age, years	63.4 + 14.8	61.3 + 14.8	0.587ª	
RRT duration, years	2.96 (0.05 – 26.1)	2.46 (0.07 – 28.0)	0.314ª	
Main causes of end-stage renal disease				
Diabetic nephropathy	126 (0.29)	176 (0.28)	0.729b	
Hypertensive nephropathy	72 (0.17)	119 (0.19)	0.371⁵	
Chronic glomerulonephritis	56 (0.13)	96 (0.15)	0.286 <sup>b</sup>	
Chronic interstitial nephritis	46 (0.11)	63 (0.10)	0.759₺	
Clinical data	n = 390	n = 565		
Coronary artery disease Myocardial infarction	128 (0.33) 63 (0.16)	229 (0.41) 139 (0.25)	0.017 <sup>b</sup> 0.002 <sup>b</sup>	
PTX, n (% of all)	16 (0.04)	12 (0.02)	0.082b	
TC, n (% of all)	68 (0.17)	85 (0.15)	0.325b	
PTX and/or TC, n (% of all)	84 (0.22)	97 (0.17)	0.094b	
Laboratory data	n = 350	n = 477		
25(OH) D (ng/mL)°	11.8 (4.51 - 50.0)	15.5 (5.10 - 30.1)	0.000003ª	
Total calcium (mg/dL)	8.94 ± 0.77	8.84 ± 0.76	0.008ª	
Phosphates (mg/dL)	5.03 (1.75 - 11.27)	5.08 (1.95 - 12.0)	0.903ª	
PTH (pg/mL)	385 (13.7 – 3,741)	376 (7.3 – 3,757)	0.896ª	
Total ALP (U/L)	99.1 (25.8 – 1,684)	92.3 (38.3 – 977)	0.003ª	
ALT (U/L)	13 (0.6 - 209)	14 (2 - 195)	0.002ª	
ASP (U/L)	15 (5 - 106)	15 (5 - 177)	0.351ª	
GGT (U/L)	25 (4 - 441)	29 (1 - 692)	0.0001ª	
Total ALP (U/L) with patients having ALT, ASP or GGT excluded <sup>d</sup>	98.3 (25.8 - 1,299)	86.5 (40.5 - 977)	0.0004°	

### Table 3.

Parameter		VDR rs2228570				
Parameter	CC	CT	TT	Odds ratio (95% CI)	P value	
Clinical data, n = 361	n = 105	n = 176	n = 80			
				CC vs CT + TT: 1.250 (0.746-2.124)	0.445	
Coronary artery disease, n (% of all)	31 (0.30)	59 (0.34)	29 (0.36)	CC + CT vs TT: 1.207 (0.689-2.087)	0.562	
				CC vs TT: 1.357 (0.696-2.639)	0.418	
				CC vs CT + TT: 1.092 (0.566-2.193)	0.919	
Myocardial infarction, n (% of all)	16 (0.15)	28 (0.16)	14 (0.18)	CC + CT vs TT: 1.143 (0.544-2.282)	0.807	
				CC vs TT: 1.180 (0.495-2.783)	0.828	
				CC vs CT + TT: 0.898 (0.279-3.384)	1.000	
Parathyroidectomy, n (% of all)	5 (0.05)	9 (0.05)	2 (0.03)	CC + CT vs TT: 0.489 (0.053-2.204)	0.543	
				CC vs TT: 0.513 (0.048-3.246)	0.696	
Treatment with cinacalcet, n (% of				CC vs CT + TT: 0.939 (0.503-1.806)	0.946	
all)	19 (0.18)	31 (0.18)	13 (0.16)	CC + CT vs TT: 0.896 (0.421-1.800)	0.894	
any				CC vs TT: 0.878 (0.370-2.031)	0.899	
Parathyroidectomy/cinacalcet, n (%				CC vs CT + TT: 1.779 (0.916-3.642)	0.095	
of all)	14 (0.13)	40 (0.23)	15 (0.19)	CC + CT vs TT: 0.970 (0.477-1.884)	1.000	
				CC vs TT: 1.500 (0.625-3.604)	0.423	
Laboratory data, n = 321	n = 93	n = 158	n = 70			
				CC vs CT + TT:	0.040a	
25(OH)D (ng/mL)	14.2 (8.1-20.7)	11.4 (4.51-18.2)	12.8 (5.8-50)	CC + CT vs TT:	0.767	
25(OH)D (lightic)	n = 19	n = 44	n = 22	CC vs TT:	0.284	
					0.204	
				CC vs CT + TT:	0.380 <sup>b</sup>	
				CC + CT vs TT:	0.131 <sup>b</sup>	
Total calcium (mg/dL)	8.89 ± 0.75	8.92 ± 0.82	9.07 ± 0.63	CC vs TT:	0.106 <sup>b</sup>	
				CC vs CT + TT:	0.239a	
			4.89 (2.48-	CC + CT vs TT:	0.627°	
Phosphorus (mg/dL)	4.79 (2.23-8.53)	5.3 (1.75-11.27)	10.96)	CC vs TT:	0.744	
			10.50)			
				00 0T - TT-	0.0003	
				CC vs CT + TT: CC + CT vs TT:	0.603° 0.291°	
PTH (pg/mL)	406.25	416	359.74		0.291	
(10,000)	(21.47-3000)	(13.72-3740.67)	(43.41-2735.5)	CC vs TT:	0.7015	
				CC vs CT + TT: 1.151 (0.593-2.322)	0.791	
PTH ≤ 150 pg/mL, n (% of all)	16 (0.17)	28 (0.18)	16 (0.23)	CC + CT vs TT: 1.394 (0.679-2.752)	0.399	
				CC vs TT: 1.426 (0.608-3.335)	0.482	
				CC vs CT + TT: 1.034 (0.616-1.744)	0.996	
PTH > 500 pg/mL, n (% of all)	38 (0.41)	69 (0.44)	26 (0.37)	CC + CT vs TT: 0.976 (0.544-1.730)	1.000	
				CC vs TT: 0.855 (0.429-1.695)	0.751	
	96	99.75	101	CC vs CT + TT:	0.396ª	
Total ALP (U/L)	(42.5-1299.33)	(25.75-1684)	(44.75-1109.5)	CC + CT vs TT:	0.671	
Total ALI (O/L)	N=80	N=138	N=61	CC vs TT:	0.428ª	
	11-00	14-130	14-01		0.420	

## Table 6.

Parameter   GG   AG   AG   AG   AG   AG   AG   A			VDR rs1544410			
Coronary artery disease, n   84 (0.41)   106 (0.40)   35 (0.40)   GG × AC × AA: 0.980 (0.680-1.414)   0.979	Parameter	GG		ΔΔ	Odds ratio (95% CI)	D value
Coronary artery disease, n (% of all)  106 (0.40)  35 (0.40)  GG vs AG + AA: 0.986 (0.880-1.414) 0.983 (0.986 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.983 (0.986) 0.984 (0.986) 0.983 (0.9	Clinical data, n = 556				Odds fado (55% Ci)	r value
Coronary artery disease, n (% of all)   106 (0.40)   35 (0.40)   GG + AG vs AA: 0.966 (0.588.1.574)   0.983 (0.78 AG   0.959 (0.556.1.643)   0.978 (0.78 AG   0.959 (0.556.1.643)   0.936 (0.78 AG   0.959 (0.556.1.643)   0.936 (0.78 AG   0.959 (0.556.1.643)   0.936 (0.78 AG   0.959 (0.		200	11 - 202	11 - 00	GG vs AG + AA: 0.980 (0.680-1.414)	0.979
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Coronary artery disease, n	84 (0.41)	106 (0.40)	35 (0.40)	· · · · · · · · · · · · · · · · · · ·	
Myocardial infarction, n (% of all patients)   G6 (0.22)   68 (0.26)   23 (0.26)   GG + AG vs AA: 1.099 (0.62-1.888)   0.814	(% of all)	04 (0.41)	100 (0.40)	33 (0.40)	GG vs AA: 0.959 (0.556-1.643)	0.978
Myocardial infarction, n (% of all patients)   G6 (0.22)   68 (0.26)   23 (0.26)   GG + AG vs AA: 1.099 (0.62-1.888)   0.514					CC -= AC - AA- 1 222 (0 001 1 000)	0.200
of all patients)  46 (0.22)  68 (0.26)  23 (0.25)  GG vs AA: 1.231 (0.856-2.266)  0.574  Parathyroidectomy, n (% of all)  Treatment with cinacalcet, n (% of all)  Parathyroidectomy/cinacal cet, n (% of all)  45 (0.17)  45 (0.17)  20 (0.23)  GG vs AG + AA: 1.866 (0.823-2.864)  GG vs AG + AA: 1.287 (0.791-2.130)  0. 127  GG vs AG + AA: 1.287 (0.791-2.130)  0. 128  GG vs AG + AA: 1.287 (0.791-2.130)  0. 129  GG vs AG + AA: 1.287 (0.791-2.130)  0. 129  GG vs AG + AA: 1.287 (0.791-2.130)  0. 129  GG vs AG + AA: 1.287 (0.791-2.130)  0. 129  GG vs AG + AA: 1.287 (0.791-2.130)  0. 129  GG vs AG + AA: 1.287 (0.791-2.130)  0. 129  GG vs AG + AA: 1.287 (0.791-2.130)  0. 129  GG vs AG + AA: 1.291 (0.834-3.299)  1. 120  GG vs AG + AA: 1.291 (0.834-3.299)  1. 120  GG vs AG + AA: 0.849 (0.834-3.299)  1. 120  GG vs AG + AA: 0.849 (0.834-3.299)  DF H ≤ 150 pg/mL, n (% of all)  21 (0.12)  37 (0.17)  21 (0.16)  GG vs AG + AA: 0.949 (0.633-1.427)  GG vs AG + AA: 0.949 (0.633-1.427)  0. 295  GG vs AG + AA: 0.949 (0.633-1.427)  0. 295  GG vs AG + AA: 0.949 (0.633-1.427)  0. 296  GG vs AG + AA: 0.949 (0.633-1.427)  0. 297  GG vs AG + AA: 0.949 (0.633-1.427)  0. 297  GG vs AG + AA: 0.949 (0.633-1.427)  0. 297  GG vs AG + AA: 0.949 (0.633-1.427)  0. 297  GG vs AG + AA: 0.949 (0.633-1.	Myocardial infarction, n (%				· · · · · · · · · · · · · · · · · · ·	
Parathyroidectomy, n (% of all)  Freatment with cinacalcet, n (% of all)  Parathyroidectomy/cinacal cet, n (%		46 (0.22)	68 (0.26)	23 (0.26)	· · · · · · · · · · · · · · · · · · ·	
Parathyroidectomy, n (% of all)  Treatment with cinacalcet, n (% of all)  Parathyroidectomy/cinacal cet, n (% of all)  A5 (0.17)  A5 (0.17)  A5 (0.17)  A5 (0.17)  A5 (0.17)  A5 (0.17)  B18 (0.20)  B18 (0.20)  B2 (0.23)  B3 (0.23)  B3 (0.23)  B3 (0.23)  B3 (0.23)  B4 (0.20)  B3 (0.23)  B3 (0.23)  B4 (0.20)  B3 (0.23)  B4 (0.20)  B3 (0.23)  B3 (0.23)  B4 (0.20)  B5 (0.24)  B5 (0.25)  B5 (0.25)  B5 (0.25)  B5 (0.25)  B5 (0.17)  B6 (0.23)  B7 (0.17)  B7 (0.17)  B7 (0.18)  B7 (0.17)  B7 (0.18)  B7 (0.17)  B7 (0.18)  B7 (0.19)  B7					GG VS AA. 1.251 (0.030-2.200)	
all)  5 (0.02)  5 (0.02)  5 (0.02)  5 (0.02)  5 (0.02)  5 (0.02)  5 (0.02)  5 (0.02)  5 (0.02)  5 (0.02)  5 (0.02)  5 (0.02)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  7 (0.015)  1 (0.02)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  7 (0.015)  7 (0.025)  8 (0.02)  8 (0.02)  6 (0.03)  8 (0.015)  1 (0.02)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  6 (0.03)  7 (0.015)  7 (0.025)  8 (0.015)  8 (0.02)  8 (0.02)  8 (0.03)  8 (0.015)  8 (0.02)  8 (0.03)  8 (0.015)  8 (0.02)  8 (0.04)  8 (0.04)  8 (0.04)  9 (0.04)  9 (0.04)  9 (0.04)  9 (0.04)  9 (0.04)  9 (0.04)  9 (0.04)  9 (0.05)  9	D					0.954
Treatment with cinacalcet, n (% of all)  Parathyroidectomy/cinacal cet, n (% of all)  Parathyroidectomy/cinacal cet, n (% of all)  Parathyroidectomy/cinacal cet, n (% of all)  131 (0.15)  45 (0.17)  20 (0.23)  63 vs AG + AA: 1.375 (0.817- 2.362)  63 vs AG + AA: 1.375 (0.817- 0.177)  23 (62 vs AG + AA: 1.566 (0.823-2.864)  63 vs AG + AA: 1.287 (0.820-2.706)  64 vs AG + AA: 1.287 (0.820-2.706)  65 vs AG + AA: 1.517 (0.822-2.706)  66 vs AG + AA: 1.517 (0.822-2.706)  67 vs AG + AA: 1.517 (0.822-2.706)  68 vs AG + AA: 1.517 (0.822-2.706)  69 vs AG + AA: 1.517 (0.822-2.706)  69 vs AG + AA: 1.517 (0.822-2.706)  60 vs AG + AA: 1.517 (0.822-2.706)  60 vs AG + AA: 1.517 (0.822-2.706)  60 vs AG + AA: 1.517 (0.822-2.706)  61 vs AG + AA: 1.517 (0.822-2.706)  62 vs AG + AA: 1.517 (0.822-2.706)  63 vs AG + AA: 1.517 (0.822-2.706)  64 vs AG + AA: 1.517 (0.822-2.706)  65 vs AG + AA: 1.517 (0.822-2.706)  66 vs AG + AA: 1.517 (0.822-2.706)  67 vs AG + AA: 1.517 (0.822-2.706)  68 vs AG + AA: 1.517 (0.822-2.706)  70 vs AG + AA: 1.517 (0.822-2.706)  71 vs AG + AA: 1.517 (0.822-2.706)  72 vs AG + AA: 1.517 (0.822-2.706)  73 vs AG + AA: 1.517 (0.822-2.706)  74 vs AG + AA: 1.517 (0.822-2.706)  75 vs AG + AA: 1.517 (0.822-2.		5 (0.02)	5 (0.02)	2 (0.02)		
Treatment with cinacalcet, n (% of all)  Parathyroidectomy/cinacal cet, n (% of all)  Parathyroidectomy/cinacal cet, n (% of all)  131 (0.15)  45 (0.17)  20 (0.23)  GG vs AA: 1.780 (0.860-3.610)  GG vs AA: 1.781 (0.823-2.706)  GG vs AA: 1.517 (0.822-2.706)  0.190  GG vs AA: 1.660 (0.834-3.239)  0.345  CG vs AA: 1.660 (0.834-3.239)  0.345  CG vs AA: 1.660 (0.834-3.239)  0.158  Laboratory data, n = 468  n = 171  n = 223  n = 74  25 (OH)D (ng/mL)  15.55 (8.6-30.1)  n = 44  15.55 (8.6-30.1)  n = 56  11.95 (5.1-24.9)  n = 16  GG vs AG + AA: (0.60 (0.834-3.239))  GG vs AG + AA: (0.823-2.706)  0.190  GG vs AA: 1.660 (0.834-3.239)  0.158  CG vs AG + AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.843-2.704)  FTH ≤ 150 pg/mL, n (% of all)  all)  FTH ≥ 500 pg/mL, n (% of all)  GG vs AG + AA: (0.814-2.707)	all)	` '	` '		GG vs AA: 0.935 (0.087-5.848)	1.000
Treatment with cinacalcet, n (% of all)  Parathyroidectomy/cinacal cet, n (% of all)  Parathyroidectomy/cinacal cet, n (% of all)  131 (0.15)  45 (0.17)  20 (0.23)  GG vs AA: 1.780 (0.860-3.610)  GG vs AA: 1.781 (0.823-2.706)  GG vs AA: 1.517 (0.822-2.706)  0.190  GG vs AA: 1.660 (0.834-3.239)  0.345  CG vs AA: 1.660 (0.834-3.239)  0.345  CG vs AA: 1.660 (0.834-3.239)  0.158  Laboratory data, n = 468  n = 171  n = 223  n = 74  25 (OH)D (ng/mL)  15.55 (8.6-30.1)  n = 44  15.55 (8.6-30.1)  n = 56  11.95 (5.1-24.9)  n = 16  GG vs AG + AA: (0.60 (0.834-3.239))  GG vs AG + AA: (0.823-2.706)  0.190  GG vs AA: 1.660 (0.834-3.239)  0.158  CG vs AG + AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.823-2.706)  0.190  GG vs AG + AG vs AA: (0.843-2.704)  FTH ≤ 150 pg/mL, n (% of all)  all)  FTH ≥ 500 pg/mL, n (% of all)  GG vs AG + AA: (0.814-2.707)					GG vs AG + AA: 1 375 ( 0 817-	0.256
n (% of all)       26 (0.13)       40 (0.15)       18 (0.20)       GG + AG vs AA: 1.566 (0.823-2.864)       0.127         GG vs AA: 1,780 (0.869.3.610)       0.345       GG vs AA: 1.780 (0.869.3.610)       0.345         Darathyroidectomy/cinacal cet, n (% of all)       31 (0.15)       45 (0.17)       20 (0.23)       GG vs AG: 1.517 (0.822-2.706)       0.190         Laboratory data, n = 468       n = 171       n = 223       n = 74         25(OH)D (ng/mL)       15.55 (8.6-30.1) n = 56       11.95 (5.1-24.9) n = 56       GG vs AG: AA: (0.25) (GG vs AG: AA: 0.025) (GG vs AG: AG: 0.137°)         Total calcium (mg/dL)       8.77 (7.15-12.25)       8.83 (6.6-10.55)       8.74 (7.25-11.7)       GG vs AG: AA: (0.845°) (GG vs AG: AG: 0.845°)         Phosphorus (mg/dL)       5.08 (1.95-10.2)       5.07 (2.03-10.45)       5.07 (2.49-11.99)       GG vs AG: AA: (0.842°) (GG vs AG: AG: 0.842°)         PTH (pg/mL)       379 (7.33-3757)       (29.53-2588)       (16.76-1847)       GG vs AG: AA: (0.842°) (GG vs AG: AG: 0.842°)         PTH ≥ 150 pg/mL, n (% of all)       21 (0.12)       37 (0.17)       12 (0.16)       GG vs AG: AA: 1.111 (0.794-2.579) (0.525°)       0.525°         PTH ≥ 500 pg/mL, n (% of all)       66 (0.39)       80 (0.36)       31 (0.42)       GG vs AG: AA: (0.1710.633-2.069) (0.531-1.427) (0.949) (0.633-1.427) (0.949) (0.633-1.427) (0.949) (0.633-1.427) (0.949) (0.633-1.427) (0.949) (0.633-1.427)	Treatment with cinacalcet.				·	
Parathyroidectomy/cinacal cet, n (% of all)   31 (0.15)   45 (0.17)   20 (0.23)   GG vs AA: 1.780 (0.860-3.610)   0.345 (0.17)   0.345 (0.17)   0.345 (0.17)   0.345 (0.15)   0.150 (0.		26 (0.13)	40 (0.15)	18 (0.20)		
Parathyroidectomy/cinacal cet, n (% of all)  20 (0.23)  31 (0.15)  45 (0.17)  20 (0.23)  31 (0.22-2.706)  32 (0.23)  33 (0.22-2.706)  34 (0.22-2.706)  35 (36 + AG vs AA: 1.517 (0.822-2.706)  36 (37 × AG: 1.660 (0.834-3.239))  36 (38 × AG: 1.660 (0.834-3.239))  37 (0.15)  28 (0.19)  38 (0.25)  45 (0.17)  29 (0.23)  30 (0.23)  30 (0.24)  30 (0.24)  31 (0.25)  31 (0.25)  31 (0.25)  31 (0.25)  32 (0.23)  33 (0.25)  34 (0.25)  35 (2.29)  36 (38 × AG: AA: (0.834-3)  36 (38 × AG: AA: (0.834-3)  37 (0.137²  38 (36 × AG: AA: (0.879²  38 (36 × AG: AA: (0.879²  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  39 (340.25)  425.38  30 (340.25)  425.38  30 (340.25)  37 (0.17)  42 (0.16)  37 (0.17)  42 (0.16)  37 (0.17)  42 (0.16)  37 (0.17)  42 (0.16)  37 (0.17)  42 (0.16)  37 (0.17)  42 (0.16)  37 (0.17)  43 (0.22)  44 (0.24)  44 (0.25)  45 (0.26)  46 (0.26)  47 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (0.26)  48 (						
$ \begin{array}{c} \text{Parathyroidectomy/cinacal cet, n (\% of all)} \\ \text{Laboratory data, n = 468} \\ \text{Database set, n (\% of all)} \\ \text{Laboratory data, n = 468} \\ \text{Database set, n (\% of all)} \\ Databas$						0.345
Laboratory data, n = 468  Laboratory data, n = 468  Laboratory data, n = 468  15.55 (8.6-30.1)  n = 44  15.55 (8.6-30.1)  n = 56  11.95 (5.1-24.9)  n = 16  GG vs AG + AA:  O.256  GG vs AG + AA:  O.777  GG + AG vs AA:  O.847  Phosphorus (mg/dL)  5.08 (1.95-10.2)  DTH (pg/mL)  379  (7.33-3757)  Total ≥ 150 pg/mL, n (% of all)  21 (0.12)  37 (0.17)  A 20 (0.36)  B 30 (0.36)  B 31 (0.42)  GG vs AG + AA:  O.526  GG vs AG + AC:  O.526  GG vs AG + AA:  O.526  O.525  GG vs AG + AA:  O.526  GG vs AG + AA:  O.526  O.525  O.526  O.525  O.526		31 (0.15)	45 (0.17)	20 (0.23)		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	cet, n (% of all)	31 (0.13)	45 (0.17)	20 (0.23)		
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	Laboratory data n = 469	n = 171	n = 222	n = 74		
25(OH)D (ng/mL)  15.55 (8.6-30.1)	Laboratory data, ii – 400	11 - 17 1			CC ve AC + AA:	0.5859
Total calcium (mg/dL)  8.77 (7.15-12.25)  8.83 (6.6-10.55)  8.74 (7.25-11.7)  GG vs AG + AA:  GG vs AG + AC:  0.777°  GG vs AG + AC:  0.845°  GG vs AG + AC:  0.879°  GG vs AG + AC:  0.842°  GG vs AG:  0.842°  GG vs AG:  0.842°  GG vs AG:  0.842°  GG vs AG:  0.841°  GG vs AG:  0.842°  GG vs AG:  0.841°  GG vs AC:  0.841°  0.841°  GG vs AC:  0.841°  0.841°  0.841°  GG vs AC:  0.841°  GG vs AC:  0.841°  0.841°  0.841°  0.841°  0.841°  GG vs AC:  0.841°  GG vs AC:  0.841°	25(OH)D (ng/mL)			11.95 (5.1-24.9)		
Total calcium (mg/dL)  8.77 (7.15-12.25)  8.83 (6.6-10.55)  8.74 (7.25-11.7)  GG vs AG + AA: GG vs AA: GG vs AG: GG vs AG: 0.879³  GG vs AG: 0.842³ GG vs AA: 0.981³  PTH (pg/mL)  7.33-3757)  7.340.25 (29.53-2588)  7.37 (0.17)  7.38 (10.17)  7.39 (10.17)  7.30 (10.17)  7.30 (10.17)  7.30 (10.17)  7.30 (10.17)  7.31 (10.12)  8.74 (7.25-11.7)  GG vs AG: AA: GG vs AG: GG v	25(OH)D (Hg/IIIL)	n = 44	n = 56	n = 16		
Total calcium (mg/dL)  8.77 (7.15-12.25)  8.83 (6.6-10.55)  8.74 (7.25-11.7)  GG + AG vs AA: GG vs AG: GG						
Phosphorus (mg/dL)	Total calcium (mg/dL)	8 77 (7 15-12 25)	8 83 (6 6-10 55)	8 74 (7 25-11 7)		
Phosphorus (mg/dL)  5.08 (1.95-10.2)  5.07 (2.03-10.45)  5.07 (2.49-11.99)  5.07 (2.49-11.99)  6G vs AG + AA: GG vs AA: GG vs AG + AA: D.801s GG vs AG + AA: D.801s GG vs AG + AA: D.81s GG vs AG + AA: D.8	rotal calcium (mg.az)	0 ( 12.25)	0.00 (0.0 10.00)	5 (1.25 1)		
Phosphorus (mg/dL)  5.08 (1.95-10.2)  5.07 (2.03-10.45)  5.07 (2.49-11.99)  GG + AG vs AA: GG vs AA: 0.842* 0.981*  PTH (pg/mL)  379 (7.33-3757)  (29.53-2588)  340.25 (29.53-2588)  (16.76-1847)  (16.76-1847)  GG vs AG + AA: GG vs AG: 0.801* GG vs AG: 0.844*  PTH ≤ 150 pg/mL, n (% of all)  21 (0.12)  37 (0.17)  12 (0.16)  FTH ≥ 500 pg/mL, n (% of all)  66 (0.39)  80 (0.36)  80 (0.36)  31 (0.42)  GG vs AG: GG vs A						
PTH (pg/mL)  379 (7.33-3757)  21 (0.12)  37 (0.17)  340.25 (29.53-2588)  425.38 (16.76-1847)  425.38 (16.76-1847)  GG vs AG + AA: GG vs AG: 0.801° 0.856 0.856 0.525  GG vs AG:	Phosphorus (mg/dL)	5.08 (1.95-10.2)	5.07 (2.03-10.45)	5.07 (2.49-11.99)		
PTH (pg/mL)    379	, , , , , , , , , , , , , , , , , , , ,	,	,	,		
PTH (pg/mL)  (7.33-3757)  (29.53-2588)  (16.76-1847)  GG + AG vs AA:  GG vs AA:  (10.801*  (16.76-1847)  GG vs AA:  (16.76-1847)  (16.76-1847)  GG vs AA:  (16.76-1847)  GG vs AA:  (16.76-1847)  (16.76-1847)  GG vs AA:  (16.76-1847)  GG vs AA:  (16.76-1847)  (16.76-1847)  GG vs AA:  (16.76-1847)  GG vs AA:  (16.76-1847)  (16.76-1847)  GG vs AA:  (16.76-1847)  (16.76-1847)  (16.76-1847)  (16.76-1847)  GG vs AA:  (16.76-1847)  (16.76-1847)  (16.76-1847)  (16.76-1847)  GG vs AA:  (16.76-1847)  (16.76-1847)  (16.76-1847)  (16.76-1847)  (16.76-1847)  (16.76-1847)  (16.76-1847)  GG vs AA:  (16.76-1847)  (16.76-1847)  (16.76-1847)  (16.76-1847)  GG vs AA:  (16.76-1847)  (16.76-1847)  (16.76-1847)  (16.76-1847)  GG vs AA:  (16.76-1847)  (16.76-1847)  (17.76-18		270	240.25	405.00	GG vs AG + AA:	0.456a
(7.33-37) (28.33-2300) (10.70-1047) GG vs AA: 0.8448 (1.411 (0.794-2.579) 0.272 (10.12) (10.12) (10.17) (12 (0.16) (10.70-1047) (10.70	PTH (pg/mL)				GG + AG vs AA:	0.801ª
PTH ≤ 150 pg/mL, n (% of all)  21 (0.12)  37 (0.17)  12 (0.16)  GG + AG vs AA: 1.121 (0.517-2.267)  GG vs AA: 1.382 (0.581-3.151)  GG vs AG + AA: 0.949 (0.633-1.427)  GG vs AG: 1.225 (0.712-2.087)  GG vs AA: 1.147 (0.632-2.069)  Total ALP (U/L)  95.8 (38.3-977.3)  91.65 (42.5-402)  80.38 (40.5-329.5)  GG + AG vs AA: 1.121 (0.517-2.087)  GG vs AG: 1.147 (0.632-2.069)  0.151³  0.223³		(1.33-3757)	(29.53-2500)	(10.76-1047)	GG vs AA:	0.844*
all)  21 (0.12) 37 (0.17) 12 (0.16) 2.267) 0.525  GG vs AA: 1.382 (0.581-3.151)  PTH ≥ 500 pg/mL, n (% of all) 80 (0.36) 31 (0.42) GG vs AA: 1.225 (0.712-2.087) 0.509  GG vs AA: 1.147 (0.632-2.069) 0.730  GG vs AG + AA: 0.949 (0.633-1.427) 0.509  GG vs AA: 1.147 (0.632-2.069) 0.730  GG vs AG + AA: 0.151³  Total ALP (U/L) 95.8 (38.3-977.3) 91.65 (42.5-402) 80.38 (40.5-329.5) GG + AG vs AA: 0.223³					GG vs AG + AA: 1.411 (0.794-2.579)	0.272
Total ALP (U/L)  SG vs AA: 1.382 (0.581-3.151)  GG vs AA: 1.382 (0.581-3.151)  GG vs AG + AA: 0.949 (0.633-1.427)  GG vs AG + AA: 0.949 (0.633-1.427)  GG vs AA: 1.147 (0.632-2.087)  GG vs AA: 1.147 (0.632-2.069)  GG vs AA: 1.147 (0.632-2.069)  GG vs AG + AA:  0.151³  GG vs AG + AA:  0.151³  O.223³	PTH ≤ 150 pg/mL, n (% of	24 (0.42)	27 (0.47)	12 (0.16)	GG + AG vs AA: 1.121 (0.517-	0.856
PTH ≥ 500 pg/mL, n (% of all)  80 (0.36)  80 (0.36)  80 (0.36)  31 (0.42)  GG vs AG + AA: 0.949 (0.633-1.427) 0.949 (0.633-1.427) 0.509 0.509 0.730  GG vs AA: 1.147 (0.632-2.069) 0.730  GG vs AG + AA: 0.949 (0.633-1.427) 0.509 0.509 0.730  GG vs AG + AA: 0.949 (0.633-1.427) 0.509 0.509 0.730  GG vs AG + AA: 0.949 (0.633-1.427) 0.509 0.509 0.730	all)	21 (0.12)	37 (U.17)	12 (0.10)	2.267)	0.525
PTH ≥ 500 pg/mL, n (% of all)  80 (0.36)  80 (0.36)  31 (0.42)  GG + AG vs AA: 1.225 (0.712-2.087) GG vs AA: 1.147 (0.632-2.069)  0.730  Total ALP (U/L)  95.8 (38.3-977.3)  91.65 (42.5-402)  80.38 (40.5-329.5)  GG + AG vs AA: 1.225 (0.712-2.087) GG vs AA: 1.147 (0.632-2.069)  0.730  0.1513  0.2233					GG vs AA: 1.382 (0.581-3.151)	
all) GG vs AA: 1.147 (0.632-2.069) 0.730  Total ALP (U/L) 95.8 (38.3-977.3) 91.65 (42.5-402) 80.38 (40.5-329.5) GG + AG vs AA: 0.223*	DTII - 500 1				· · · · · · · · · · · · · · · · · · ·	
GG vs AA: 1.147 (0.632-2.069) 0.730  GG vs AA: 1.147 (0.632-2.069) 0.730  GG vs AG + AA: 0.151a  Total ALP (U/L) 95.8 (38.3-977.3) 91.65 (42.5-402) 80.38 (40.5-329.5) GG + AG vs AA: 0.223a		66 (0.39)	80 (0.36)	31 (0.42)		
Total ALP (U/L) 95.8 (38.3-977.3) 91.65 (42.5-402) 80.38 (40.5-329.5) GG + AG vs AA: 0.223 <sup>a</sup>	all)				GG vs AA: 1.147 (0.632-2.069)	0.730
Total ALP (U/L) 95.8 (38.3-977.3) 91.65 (42.5-402) 80.38 (40.5-329.5) GG + AG vs AA: 0.223 <sup>a</sup>					GG vs AG + AA:	0.151
	Total ALP (U/L)	95.8 (38.3-977.3)	91.65 (42.5-402)	80.38 (40.5-329.5)		
	(-1			(11121111111111111111111111111111111111		

## Table 9.

Parameter		RXRA rs10881	578		
Faranietei	AA	AG	GG	Odds ratio (95% CI)	P value
Clinical data, n = 563	n = 273	n = 236	n = 54		
Coronany artery diagona n /9/ of				AA vs AG + GG: 0.852 (0.600-1.210)	0.396
Coronary artery disease, n (% of all)	116 (0.43)	87 (0.37)	25 (0.46)	AA + AG vs GG: 1.299 (0.707-2.372)	0.441
all)				AA vs GG: 1.167 (0.619-2.184)	0.712
Myocardial infarction, n (% of all				AA vs AG + GG: 1.230 (0.823-1.844)	0.338
patients)	62 (0.23)	57 (0.24)	20 (0.37)	AA + AG vs GG: 1.928 (1.010-3.592)	0.047
Jacients)				AA vs GG: 2.002 (1.013-3.867)	0.046
				AA vs AG + GG: 1.908 (0.504-8.750)	0.444
Parathyroidectomy, n (% of all)	4 (0.02)	8 (0.03)	0 (0.00)	AA + AG vs GG: 0.000 (0.000-3.420)	0.589
				AA vs GG: 0.000 (0.000-7.729)	0.968
Froatment with cinecalest # 49/				AA vs AG + GG: 1.339 (0.819-2.201)	0.266
Freatment with cinacalcet, n (% of all)	36 (0.13)	43 (0.18)	6 (0.11)	AA + AG vs GG: 0.680 (0.230-1.668)	0.524
л ап)				AA vs GG: 0.823 (0.269-2.124)	0.875
Parathuraidaatamu/ainaaalaat n				AA vs AG + GG: 1.425 (0.895-2.283)	0.144
Parathyroidectomy/cinacalcet, n	40 (0.15)	51 (0.22)	6 (0.11)	AA + AG vs GG: 0.574 (0.195-1.401)	0.285
% of all)				AA vs GG: 0.728 (0.239-1.865)	0.659
aboratory data, n = 476	n = 233	n = 199	n = 44		
	15.59 ± 4.09	15.22 ± 5.24	16.08 ± 3.91	AA vs AG + GG:	0.805
25(OH)D (ng/mL)	n = 58	n = 49	n = 12	AA + AG vs GG:	0.635b
	11 - 30	11 - 43	11 - 12	AA vs GG:	0.705
	0.70 (0.0			AA vs AG + GG:	0.048
Fotal calcium (mg/dL)	8.72 (6.6-	8.9 (6.8-12.3)	9.0 (7.3-11.3)	AA + AG vs GG:	0.088
	11.7)			AA vs GG:	0.0426
				AA vs AG + GG:	0.793ª
Phosphorus (mg/dL)	5.1 (2.5-10.5)	5.1 (2-12)	4.9 (2-9.3)	AA + AG vs GG:	0.390
				AA vs GG:	0.404
	349.3	419.8	322.5	AA vs AG + GG:	0.186ª
PTH (pg/mL)	(16.8-2991.5)	(7.3-3757)	(65.8-2570)	AA + AG vs GG:	0.386a
	(10.0-2991.5)	(1.3-3131)	(03.0-2370)	AA vs GG:	0.644ª
				AA vs AG + GG: 1.016 (0.596-1.734)	1.000
PTH ≤ 150 pg/mL, n (% of all)	35 (0.15)	27 (0.14)	10 (0.23)	AA + AG vs GG: 1.755 (0.734-3.862)	0.215
				AA vs GG: 1.664 (0.670-3.838)	0.295
				AA vs AG + GG: 1.288 (0.874-1.899)	0.214
PTH > 500 pg/mL, n (% of all)	82 (0.35).	83 (0.42)	17 (0.39)	AA + AG vs GG: 1.019 (0.504-2.007)	1.000
				AA vs GG: 1.159 (0.558-2.355)	0.783
	00.4	04.4	96.4	AA vs AG + GG:	0.925a
otal ALP (U/L)	90.1	94.4	86.4	AA + AG vs GG:	0.609ª
	(38.3-977.3)	(42.5-859.5)	(45-692.3)	AA vs GG:	0.697

Conclusions

Our aim was to evaluate a frequency distribution of vitamin D pathway gene polymorphisms in hemodialysis (HD) women and men in relation to prevalence of coronary artery disease (CAD) and severity of secondary hyperparathyroidism (sHPT).

### Table 1.

RXRA HD women		Control women O	Odds ratio (95%CI)	Two-	P <sub>trend</sub>	P <sub>genotyping</sub>	Power	P for deviation from HWE and expected genotype frequencies	
	(frequency)	(frequency)		Р	55/13	gonotyping	(%)	HD women	Control women
rs10776909	n = 429	n = 163						0.706	0.931
CC	262 (0.61)	115 (0.71)	Referenta	-	0.026	0.081		263 (0.61)	115 (0.71)
СТ	149 (0.35)	44 (0.27)	1.486 (0.980-2.278)	0.063			47.8	146 (0.34)	44 (0.27)
π	19 (0.04)	4 (0.02)	2.085 (0.671-8.601)	0.268			31.1	20 (0.05)	4 (0.02)
ст+тт	168 (0.39)	48 (0.29)	1.536 (1.026-2.319)	0.036			57.2		
MAF	187 (0.22)	52 (0.16)	1.468 (1.038-2.102)	0.029			61.1		
rs10881578	n = 428	n = 163						0.527	0.876
AA	225 (0.53)	88 (0.54)	Referent	-	0.675	0.901		222 (0.52)	88 (0.54)
AG	167 (0.39)	63 (0.39)	1.037 (0.697-1.547)	0.931			4.6	172 (0.40)	64 (0.39)
GG	36 (0.08)	12 (0.07)	1.173 (0.565-2.594)	0.797			5.6	33 (0.08)	12 (0.07)
AG+GG	203 (0.47)	75 (0.46)	1.059 (0.726-1.546)	0.829			5.2		
MAF	239 (0.28)	87 (0.27)	1.064 (0.792-1.437)	0.729			6.4		
rs749759	n = 411	n = 160						0.780	0.551
GG	226 (0.55)	94 (0.59)	Referent	-	0.311	0.563		227 (0.55)	95 (0.60)
AG	159 (0.39)	59 (0.37)	1.121 (0.751-1.679)	0.629			7.9	157 (0.38)	56 (0.35)
AA	26 (0.06)	7 (0.04)	1.545 (0.625-4.360)	0.438			12.1	27 (0.07)	8 (0.05)
AG+AA	185 (0.45)	66 (0.41)	1.166 (0.793-1.720)	0.472			12.4		
MAF	211 (0.26)	73 (0.23)	1.168 (0.854-1.609)	0.355			15.9		

### Table 4.

Doromotor	R)	(RA rs1077690	9		
Parameter	CC	CT	TT	Odds ratio (95% CI)	P value
Clinical data, n = 388	n = 235	n = 134	n = 19		
Coronary artery disease, n (%				CC vs CT + TT: 1.098 (0.695-1.730)	0.752
	75 (0.32)	40 (0.30)	12 (0.63)	CC + CT vs TT: 3.786 (1.329-11.62)	0.010
of all)				CC vs TT: 3.657 (1.261-11.37)	0.014
Augustian m /0/ of				CC vs CT + TT: 1.547 (0.861-2.770	0.154
Myocardial infarction, n (% of	32 (0.14)	24 (0.18)	6 (0.32)	CC + CT vs TT: 2.580 (0.768-7.628)	0.129
all)				CC vs TT: 2.928 (0.845-8.957)	0.092
				CC vs CT + TT: 0.688 (0.184-2.204)	0.684
arathyroidectomy, n (% of all)	11 (0.05)	5 (0.04)	0 (0.00)	CC + CT vs TT: 0.000 (0.000-5.273)	0.881
,	()	- ()	- ()	CC vs TT: 0.000 (0.000-5.127)	0.835
				CC vs CT + TT: 0.636 (0.345-1.146)	0.144
Freatment with cinacalcet, n (%	47 (0.20)	24 (0.46)	0.70.000	CC + CT vs TT: 0.000 (0.000-0.979)	0.047
of all)	47 (0.20)	21 (0.16)	0 (0.00)	CC vs TT: 0.000 (0.000-0.899)	0.035
Parathyroidectomy/cinacalcet,				CC vs CT + TT: 0.625 (0.357-1.073)	0.093
n (% of all)	58 (0.25)	26 (0.19)	0 (0.00)	CC + CT vs TT: 0.000 (0.000-0.748)	0.017
1 (70 Of all)				CC vs TT: 0.000 (0.000-0.682)	0.012
Laboratory data, n = 349	n = 213	n = 119	n = 17		
	11.65	12.3	13.6	CC vs CT + TT:	0.788
25(OH)D (ng/mL)	(5.8-50)	(6.6-18.9)	(4.51-18.4)	CC + CT vs TT:	0.718ª
	n = 58	n = 26	n = 4	CC vs TT:	0.763ª
	8.9 (6.7-11.4)	9.0 (6.0-10.9)	9.07 (7.7- 10.8)	CC vs CT + TT:	0.555*
Fotal calcium (mg/dL)				CC + CT vs TT:	0.403
				CC vs TT:	0.342b
	5.1	5.0	4.5	CC vs CT + TT:	0.372ª
Phosphorus (mg/dL)	(2.2-11.3)	(2.5-9.0)	(1.8-9.3)	CC + CT vs TT:	0.102ª
	(2.2 11.0)	(2.5 5.5)	(	CC vs TT:	0.094
	413	373	236.3	CC vs CT + TT:	0.296
PTH (pg/mL)		(38.4-2266.7)	(13.7-821)	CC + CT vs TT:	0.144ª
	(	(,	· · · · · · · · · · · · · · · · · · ·	CC vs TT:	0.126ª
				CC vs CT + TT: 0.818 (0.454-1.449)	0.557
PTH ≤ 150 pg/mL, n (% of all)	46 (0.22)	21 (0.18)	4 (0.24)	CC + CT vs TT: 1.217 (0.280-4.104)	0.934
				CC vs TT: 1.117 (0.253-3.844)	1.000
				CC vs CT + TT: 0.691 (0.432-1.101)	0.126
PTH ≥ 500 pg/mL, n (% of all)	94 (0.44)	44 (0.37)	4 (0.24)	CC + CT vs TT: 0.433 (0.101-1.442)	0.217
,	(,		. ()	CC vs TT: 0.390 (0.090-1.320)	0.157
				CC vs CT + TT:	0.155°
Total ALP (U/L)	102	95.3	116.4	CC + CT vs TT:	0.234
out the (ore)	(25.8-1684)	(41.3-579)	(64.8-241)	CC vs TT:	0.398

Parameter		VDR rs2228570			
Parameter	CC	CT	Π	Odds ratio (95% CI)	P val
Clinical data, n = 543	n = 145	n = 292	n = 106		
Coronary artery disease, n				CC vs CT + TT: 0.799 (0.534-1.198)	0.29
% of all)	64 (0.44)	116 (0.40)	38 (0.36)	CC + CT vs TT: 0.798 (0.499-1.264)	0.37
70 GT GII)				CC vs TT: 0.707 (0.408-1.220)	0.23
Myocardial infarction, n (%		22 /2 2 //		CC vs CT + TT: 0.871 (0.553-1.389)	0.60
of all)	38 (0.26)	69 (0.24)	25 (0.24)	CC + CT vs TT: 0.951 (0.553-1.598)	0.95
				CC vs TT: 0.869 (0.463-1.613)	0.74
Parathyroidectomy, n (% of	0 (0 00)	0 (0 00)	0 (0 00)	CC vs CT + TT: 1.095 (0.268-6.376)	1.00
all)	3 (0.02).	6 (0.02)	3 (0.03)	CC + CT vs TT: 1.385 (0.237-5.675)	0.85
				CC vs TT: 1.379 (0.181-10.49)	1.00
reatment with cinacalcet, n	24 (0.44)	44 (0.45)	40 (0 47)	CC vs CT + TT: 1.090 (0.624-1.964)	0.86
% of all)	21 (0.14)	44 (0.15)	18 (0.17)	CC + CT vs TT: 1.171 (0.621-2.120)	0.68
				CC vs TT: 1.208 (0.570-2.536)	0.71
Parathyroidectomy/cinacalc	24 (0.47)	ED (D 47)	24 (0.20)	CC vs CT + TT: 1.095 (0.646-1.905)	0.83
et, n (% of all)	24 (0.17)	50 (0.17)	21 (0.20)	CC + CT vs TT: 1.212 (0.670-2.123)	0.56
aboratory data, n = 455	n = 120	n = 241	n = 94	CC vs TT: 1.246 (0.615-2.503)	0.6
aboratory data, ii = 455	11 = 120	11 = 241	11 = 94	CC vs CT + TT:	
	15.34 ± 4.54	15.56 ± 4.43	15.65 ± 5.25	CC + CT vs TT:	0.803b
25(OH)D (ng/mL)	n = 33	n = 65	n = 20	CC vs TT:	0.8826
	11 = 33	11 = 65	H = 20	CC VS 11.	0.823b
				CC vs CT + TT:	0.036ª
				CC + CT vs TT:	0.422ª
「otal calcium (mg/dL)	8.92 (7.5-10.58)	8.72 (6.8-12.25)	8.80 (6.6-10.27)	CC vs TT:	0.069
				55 15 11.	0.000
				CC vs CT + TT:	0.192ª
				CC + CT vs TT:	0.167°
Phosphorus (mg/dL)	4.85 (1.95-10.45)	5.06 (2.03-11.99)	5.15 (2.85-10.2)	CC vs TT:	0.088
				CC vs CT + TT:	0.988ª
TH (mm/ml)	384.88	367.03	377.68	CC + CT vs TT:	0.489a
PTH (pg/mL)	(29.53-3757)	(7.33-2435)	(16.76-2350.5)	CC vs TT:	0.690
TH < 450 paint = 19/ of				CC vs CT + TT: 0.605 (0.340-1.099)	0.102
PTH ≤ 150 pg/mL, n (% of	24 (0.20)	33 (0.14)	11 (0.12)	CC + CT vs TT: 0.707 (0.320-1.441)	0.412
ill)				CC vs TT: 0.530 (0.221-1.208)	0.147
TH > 500 pg/ml = 200 of				CC vs CT + TT: 0.995 (0.635-1.568)	1.000
PTH ≥ 500 pg/mL, n (% of	46 (0.38)	88 (0.37)	40 (0.43)	CC + CT vs TT: 1.255 (0.768-2.038)	0.397
all)					0.628
				CC vs CT + TT:	0.62
Total ALP (U/L)	87 (49-977.25)	95.75 (38.25-	91.75 (42.5-	CC + CT vs TT:	0.62
otal ALP (O/L)	01 (49-911.25)	692.33)	425.25)	CC vs TT:	0.71

# Methods:

HD women (n = 431, age 63.4 + 14.8 years) and men (n = 625, age 61.3 + 14.8 years) as well as control women (n = 163, age 49.5 + 12.7 years) and men (n = 150, age 48.9 + 12.4 years) were enrolled into the study.

Polymorphisms of genes encoding vitamin D binding protein (GC): rs2298849 (genotyped by High Resolution Melt analysis - HRM), rs7041 (Restriction Fragment Length Polymorphism analysis - RFLP, restriction enzyme - HaeIII), rs1155563 (HRM), vitamin D receptor (VDR): rs2228570 (RFLP, Fokl), rs1544410 (RFLP, Fspl), and retinoid x receptor A (RXRA): rs10776909 (HRM), rs10881578 (HRM), rs749759 (RFLP, BstXI) were genotyping in all study subjects. Frequency distributions of the respective genotypes were compared between groups with and without age matching.

Clinical data [prevalence of CAD, myocardial infarction (MI), parathyroidectomy (PTX), and treatment of cinacalcet (TC), 955 patients reviewed for each parameter] and laboratory results [serum Ca, P, ALP, and PTH, 827 mean values of 2-4 results for each parameter; plasma 25(OH)D, 210 determinations] were compared in HD women and men bearing different polymorphic variants of the analyzed genotypes. In patients who underwent PTX or TC, laboratory data shown before these treatment commencements were taken into analysis.

### Table 2.

Parameter		GC rs7041		P	
Parameter	GG	GT	Π	Odds ratio (95% CI)	
Clinical data, n = 366	n = 125	n = 188	n = 53		valu
				GG vs GT + TT: 0.735 (0.456-1.191)	0.22
Coronary artery disease, n (% of all)	47 (0.38)	58 (0.31)	16 (0.30)	GG + GT vs TT: 0.857 (0.424-1.666)	0.75
				GG vs TT: 0.718 (0.335-1.497)	0.44
				GG vs GT + TT: 0.754 (0.409-1.412)	0.41
Myocardial infarction, n (% of all)	23 (0.18)	28 (0.15)	7 (0.13)	GG + GT vs TT: 0.782 (0.282-1.879)	0.73
				GG vs TT: 0.675 (.228-1.778)	0.53
				GG vs GT + TT: 2.319 (0.619-12.90)	0.28
Parathyroidectomy, n (% of all)	3 (0.02)	9 (0.05)	4 (0.08)	GG + GT vs TT: 2.048 (0.462-7.099)	0.37
				GG vs TT: 3.320 (0.536-23.32)	0.23
				GG vs GT + TT: 1.017 (0/560-1.887)	1.00
Freatment with cinacalcet, n (% of all)	22 (0.18)	35 (0.19)	8 (0.15)	GG + GT vs TT: 0.798 (0.308-1.836)	0.74
				GG vs TT: 0.832 (0.298-2.128)	0.8
Parathyroidectomy/cinacalcet, n (%				GG vs GT + TT: 0.944 (0.532-1.702)	0.9
of all)	25 (0.20)	34 (0.18)	12 (0.23)	GG + GT vs TT: 1.260 (0.567-2.630)	0.6
				GG vs TT: 1.171 (0.487-2.694)	0.83
aboratory data, n = 327	n = 113	n = 165	n = 49		
	12.6 (8.0 – 50.0)	11.8 (4.5 - 20.3)	11.3 (5.8 - 15.7)	GG vs GT + TT:	0.15
25(OH) D (ng/mL)	n = 32	n = 42	n = 17	GG + GT vs TT:	0.0
	11 - 32	11 - 42	11-17	GG vs TT:	0.0
				GG vs GT + TT:	0.60
otal calcium (mg/dL)	8.93 (6.01 - 10.4)	8.94 (6.80 - 11.4)	9.15 (6.65 - 10.4)	GG + GT vs TT:	0.64
				GG vs TT:	0.68
				GG vs GT + TT:	0.22
hosphates (mg/dL)	5.03 (1.75 - 9.33)	4.80 (2.23 - 11.3)	5.58 (3.40 - 8.97)	GG + GT vs TT:	0.00
				GG vs TT:	0.00
				GG vs GT + TT:	0.14
TH (pg/mL)	331 (13.7 – 3,741)	433 (38.4 – 2,736)	411 (36.3 - 2,267)	GG + GT vs TT:	0.42
				GG vs TT:	0.24
				GG vs GT + TT:	0.84
otal ALP (U/L)	98.4 (42.8 – 1,684)	98.2 (25.8 – 1,110)	104 (42.5 - 579)	GG + GT vs TT:	0.73
				GG vs TT:	0.88

### Table 5.

Parameter		RXRA rs10881578			
	AA	AG	GG	Odds ratio (95% CI)	P valu
Clinical data, n = 389	n = 211	n = 142	n = 36		
				AA vs AG + GG: 1.231 (0.787-1.922)	0.395
Coronary artery disease, n (% of all)	65 (0.31)	50 (0.35)	13 (0.36)	AA + AG vs GG: 1.170 (0.524-2.509)	0.795
				AA vs GG: 1.270 (0.554-2.803)	0.651
Muse and inferation in 10/ of all				AA vs AG + GG: 1.273 (0.715-2.267)	0.460
Myocardial infarction, n (% of all	31 (0.15)	26 (0.18)	6 (0.17)	AA + AG vs GG: 1.039 (0.338-2.693)	0.139
patients)				AA vs GG: 1.161 (0.365-3.158)	0.923
				AA vs AG + GG: 1.552 (0.502-5.009)	0.544
Parathyroidectomy, n (% of all)	7 (0.03)	7 (0.05)	2 (0.06)	AA + AG vs GG: 1.424 (0.151-6.614)	0.893
	,	` '	,	AA vs GG: 1.714 (0.167-9.500)	0.774
				AA vs AG + GG: 0.923 (0.524-1.614)	0.871
Treatment with cinacalcet, n (% of	38 (0.18)	20 (0.14)	10 (0.28)	AA + AG vs GG: 1.956 (0.796-4.465)	0.150
all)	(	,	, , , , , , , , , , , , , , , , , , , ,	AA vs GG: 1.751 (0.692-4.138)	0.257
				AA vs AG + GG: 1.035 (0.618-1.728)	0.986
Parathyroidectomy/cinacalcet, n (%	45 (0.21)	27 (0.19)	12 (0.33)	AA + AG vs GG: 1.951 (0.845-4.282)	0.122
of all)	(5.2.)	27 (5.10)	.2 (3.33)	AA vs GG: 1.844 (0.775-4.184)	0.178
Laboratory data, n = 350	n = 186	n = 130	n = 34	70110 00. 1.017 (0.110 1.101)	
Laboratory data; ii coc				AA vs AG + GG:	0.512
25(OH)D (ng/mL)	11.9 (5.8-50)	11.9 (7-18.9)	11.2 (4.51-18.4)	AA + AG vs GG:	0.149
zo(on)o (ng.mz)	n = 46	n = 35	n = 7	AA vs GG:	0.184
				AA vs AG + GG:	0.687
Total calcium (mg/dL)	8.95 (6.0-10.9)	8.98 (7-11.4)	8.87 (7.4-9.9)	AA + AG vs GG:	0.321
rotal calcium (ing. az)	0.00 (0.0 10.0)	0.00 (1 11.1)	0.07 (777 0.0)	AA vs GG:	0.305
				AA vs AG + GG:	0.331
Phosphorus (mg/dL)	5.2 (2.2-10.95)	4.8 (1.8-11.3)	5.3 (2.6-8.7)	AA + AG vs GG:	0.702
i nospilorus (mg/uz)	5.2 (2.2-10.55)	4.0 (1.0-11.0)	0.0 (2.0-0.1)	AA vs GG:	0.981
				AA vs AG + GG:	0.127
PTH (pg/mL)	432.6 (19.5-3000)	306.4 (13.7-3740.7)	387.98 (45.2-2266.7)	AA + AG vs GG:	0.649
r III (pg/IIIc)	432.0 (13.3-3000)	300.4 (13.7-3740.7)	307.30 (43.2-2200.7)	AA vs GG:	0.996
				AA vs AG + GG: 1.053 (0.603-1.835)	0.950
PTH ≤ 150 pg/mL, n (% of all)	37 (0.20)	28 (0.22)	6 (0.18)	AA + AG vs GG: 0.828 (0.269-2.153)	0.887
FTIT'S 150 pg/mc, if (% of all)	37 (0.20)	20 (0.22)	0 (0.10)	AA vs GG: 0.863 (0.272-2.338)	0.973
DTH > 500 palml - p. (% of all)	96 (0.46)	44 (0.22)	15 (0.44)	AA vs AG + GG: 0.603 (0.382-0.950)	0.028
PTH ≥ 500 pg/mL, n (% of all)	86 (0.46)	41 (0.32)	15 (0.44)	AA + AG vs GG: 1.175 (0.534-2.541)	0.789
				AA vs GG: 0.918 (0.407-2.039)	0.970
Total ALD (IIII.)	402 5 (25 0 4200 2)	04 5 (44 2 4004)	00.0 (40.500.0)	AA vs AG vs GG	0.020
Total ALP (U/L)	103.5 (25.8-1299.3)	94.5 (41.3-1684)	99.8 (49-500.8)	AA + AG vs GG:	0.729
				AA vs GG:	0.717

# Table 8.

Parameter		XRA rs1077690	)9		
Faranietei	CC CT		TT	Odds ratio (95% CI)	P value
Clinical data, n = 565	n = 341	n = 146	n = 29		
C				CC vs CT + TT: 1.205 (0.821-1.766)	0.365
Coronary artery disease,	146 (0.43)	69 (0.47)	14 (0.48)	CC + CT vs TT: 1.181 (0.516-2.687)	0.804
n (% of all)		()		CC vs TT: 1.247 (0.539-2.866)	0.704
				CC vs CT + TT: 1.463 (0.956-2.228)	0.081
Myocardial infarction, n	83 (0.24)	45 (0.31)	11 (0.)	CC + CT vs TT: 1.714 (0.710-3.949)	0.250
(% of all)	00 (0.21)	10 (0.01)	(0.)	CC vs TT: 1.900 (0.776-4.441)	0.171
				CC vs CT + TT: 1.403 (0.346-5.220)	0.769
Parathyroidectomy, n (%	7 (0.02)	3 (0.02)	2 (0.07)	CC + CT vs TT: 3.533 (0.358-17.76)	0.284
of all)	7 (0.02)	3 (0.02)	2 (0.07)	CC vs TT: 3.534 (0.340-19.72)	0.303
				CC vs CT + TT: 2.065 (1.250-3.399)	0.004
Treatment with	44 (0.42)	20 (0.25)	E (0.47)	CC + CT vs TT: 1.060 (0.307-2.949)	1.000
cinacalcet, n (% of all)	44 (0.13)	36 (0.25)	5 (0.17)	CC vs TT: 1.406 (0.398-4.027)	0.670
Parathyroidectomy/cinac				CC vs CT + TT: 2.028 (1.259-3.254)	0.003
alcet, n (% of all)	51 (0.15)	39 (0.27)	7 (0.24)	CC + CT vs TT: 1.404 (0.491-3.533)	0.585
				CC vs TT: 1.809 (0.619-4.671)	0.298
Laboratory data, n = 477	n = 288	n = 162	n = 27		
	15.57 ± 4.83 n = 79	15.16 ± 4.11 n = 37	17.3 ± 2.11 n = 3	CC vs CT + TT:	0.777₺
25(OH)D (ng/mL)				CC + CT vs TT:	0.487⁵
				CC vs TT:	0.540b
		8.8 (7.2-11.6)	9.1 (8.3-12.3)	CC vs CT + TT:	0.329ª
Total calcium (mg/dL)	8.8 (6.6-11.7)			CC + CT vs TT:	0.011
				CC vs TT:	0.010a
				CC vs CT + TT:	0.628a
Phosphorus (mg/dL)	5.0 (1.9-10.5)	5.1 (2-12)	5.1 (3.3-9.3)	CC + CT vs TT:	0.744ª
				CC vs TT:	0.673ª
	340.8 (16.8-	424.2 (12.7-	320 1 /7 3	CC vs CT + TT:	0.188
PTH (pg/mL)	3757)	2991.5)	329.1 (7.3-	CC + CT vs TT:	0.657
	3/3/)	2551.5)	2181.2)	CC vs TT:	0.849
DTH < 450 polml = 20/ of				CC vs CT + TT: 1.228 (0.716-2.092)	0.501
PTH ≤ 150 pg/mL, n (% of	41 (0.14)	27 (0.17)	5 (0.19)	CC + CT vs TT: 1.277 (0.365-3.614)	0.797
all)				CC vs TT: 1.369 (0.383-3.988)	0.713
					2.15
PTH ≥ 500 pg/mL, n (% of				CC vs CT + TT: 1.389 (0.936-2.058)	0.107
all)	101 (0.35)	71 (0.44)	10 (0.37)	CC + CT vs TT: 0.951 (0.380-2.258)	1.000
any				CC vs TT: 1.089 (0.429-2.629)	0.991
	91 (38.3-	92.9 (40.5-		CC vs CT + TT:	0.831°
Total ALP (U/L)	859.5)	977.3)	88 (45.7-379)	CC + CT vs TT:	0.913
	555.57	511157		CC vs TT:	0.900

# Summary of the genetic results

Comparisons to controls

HD women compared to healthy women differed in a frequency distribution of rs10776909 independently on whether age matched or not (Table 1). HD men compared to healthy men did not differ in the frequency distribution of vitamin D pathway gene polymorphism independently on whether age matched or not (Ptrend > 0.05).

# Comparisons between HD women and HD men

HD women and men did not differ in a frequency distribution of vitamin D pathway gene polymorphisms, also if age pair matched subjects were compared which additionally did not differ in RRT vintage and main causes of ESRD (Ptrend > 0.05).

# HD women

GC rs7041: TT genotype was associated with lower 25(OH)D plasma levels and higher serum phosphorus levels (Table 2).

VDR rs2228570: Lower 25(OH)D plasma levels were in CT+TT compared to CC carriers (Table 3).

RXRA rs10776909: TT genotype was associated with higher prevalence of CAD; CC genotype was associated with higher frequency of treatment with cinacalcet and PTX/cinacalcet (Table 4).

RXRA rs10881578: AA women had higher prevalence of PTH ≥ 500 pg/mL (P = 0.028) and higher ALP activity (P = 0.020) than AG+GG women (Table 5). HD men

VDR rs1544410: Lower 25(OH)D plasma levels were in AA compared to GG+AG carriers (Table 6).

VDR rs2228570: Higher Ca levels were shown in CC compared to TT carriers (Table 7),

RXRA rs10776909: TT genotype was associated with higher serum levels of total calcium. CC carriers were less frequently treated with cinacalcet and PTX/cinacalcet than CC+TT carriers (Table 8).

RXRA rs10881578: GG genotype was associated with higher prevalence of MI; AA genotype was associated with associated with lower concentrations of total calcium (Table 9).

In HD patients there are associations between vitamin D pathway gene polymorphisms, CAD/MI prevalence, mineral disorders, and severity of sHPT. Gender related factors may be important in expression of associations between vitamin D pathway polymorphic variants and mentioned abnormalities.





