Predictive value of traditional and novel risk factors for cardiovascular disease and end stage renal disease in patients with chronic kidney disease

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Objetives:

Up to 25% of mild to moderate chronic kidney disease (CKD) patients die from cardiovascular (CV) disease before entering dialysis, whereas control of CKD progression risk factors remains a bet to be won by nephrologists

The predictive value of traditional and novel risk factors is important because the identification of "the best predictor" is of obvious importance for risk stratification in CKD patients

The **aim** of this prospective study was to evaluate the predictive value of several traditional and potential novel risk factors for CV disease and end stage renal disease (ESRD) in CKD patients of stages 1-4

Methods:

- **230** consecutive CKD outpatients of stages 1-4 were prospectively followed up for 3 years
- Patients lost of follow up were excluded, finally 189 pts were analyzed
- Demographic, somatometric and clinical characteristics, co-morbidities, biochemical markers and specific markers reflecting inflammation and endothelial dysfunction were assessed at study entry (Table 1)
- Echocardiograms were undertaken and left ventricular mass index (LVMI) was calculated (Table 1)

Major end points:
- CV death and non-fatal CV events [myocardial infarction, angina, requirement of coronary intervention (angioplasty, coronary artery bypass or pacemaker placement), cerebrovascular (ischemic or hemorrhagic stroke) or peripheral vascular disease]
- Initiation of dialysis (no preemptive kidney transplantation occurred)

Statistical analysis
- Cox regression proportional hazard models were used to determine factors that best predicted the occurrence of a CV event/death or initiation of dialysis
- Models included traditional and novel risk factors: age, sex, smoking, body mass index, mean BP, diabetes mellitus (DM), CV disease history, eGFR-MDRD, urine protein (UPR), serum cholesterol, albumin, uric acid and phosphorus, Hb, fibrinogen, CRP, IL-6, TNF-α, ICAM-1, VCAM-1 and LVMI

Table 1: Baseline characteristics of the CKD patients stages 1-4 (3 groups)

	All	No event	CVD event/death	ESRD (dialysis)	P-value
Number (%)	189	130 (68.8)	38 (20.1)	21 (11.1)	
Age, years	68 (60.7-73.3)	66 (58.6-73)	71 (65-74.2)	71 (53.5-73.3)	0.006
Male, n(%)	95 (50.3)	60 (46.2)	25 (65.8)	10 (47.6)	
Smokers, n(%)	32 (16.9)	25 (19.2)	2 (5.3)	5 (23.8)	
eGFR - MDRD, ml/min/1.73m²	46.7 (28.4-73)	55.3 (36.7-76)	40.8 (24.2-63.4)	21 (16-26.8)	<0.001
Urine protein, mg/24h	306 (140-1008)	214 (124-533)	394 (159-1829)	2310 (700-5486)	<0.001
Diabetes mellitus, n(%)	59 (31.2)	32 (24.6)	18 (47.4)	9 (42.9)	0.01
Hypertension, n(%)	169 (89.4)	115 (88.5)	36 (94.7)	18 (85.7)	
History of CVD, n(%)	55 (29.3)	34 (26.2)	16 (42.1)	5 (25)	
BMI, kg/m²	29.2 (5.3)	29.4 (5.3)	29.2 (5.3)	27.9 (5.0)	
Mean BP, mmHg	100 (10.7)	100.5 (10.2)	98.3 (11.7)	100.5 (11.8)	
Total Cholesterol, mg/dl	210 (43)	214 (40)	197 (42)	213 (55)	
Hb, g/l	13.3 (1.6)	13.5 (1.6)	12.9 (1.7)	12.6 (1.0)	0.002
Serum Biochemical markers					
Albumin, g/l	4.2 (4.1-4.4)	4.3 (4.1-4.4)	4.2 (3.9-4.2)	4.1 (4.0-4.3)	0.001
Uric Acid, mg/dl	6.6 (1.6)	6.5 (1.6)	6.7 (1.6)	7.0 (1.6)	
Phosphorus, mg/dl	3.4 (0.7)	3.3 (0.6)	3.5 (0.7)	4.2 (0.9)	<0.001
Inflammatory/Endothelial dysfunction					
CRP, mg/l	2.0 (0.7-4.4)	2.0 (0.8-4.2)	1.2 (0.5-4.2)	2.0 (1.0-5.4)	
Fibrinogen, mg/dl	372.5 (317.3-449)	367 (313.3-430)	381.5 (322-499.8)	409 (333.3-620)	
IL-6, pg/ml	3.0 (2-4.4)	2.7 (1.9-4.1)	4.1 (2.9-6.3)	3.2 (2.2-4.0)	0.01
TNF-α, pg/ml	1.9 (1.4-2.8)	1.8 (1.4-2.7)	2.1 (1.7-2.7)	2.3 (1.7-3.2)	
ICAM-1, pg.ml	253.5 (201-329.7)	247 (200-316.8)	268.5 (182-356.5)	252.5 (219.5-380)	
VCAM-1, pg/ml	852 (625.8-1164.5)	750 (589.8-1039.7)	1023 (834.5-1478.6)	1061.5 (937-1457.8)	<0.001
LVMI, g/m²	138.7 (46.7)	128.6 (41.3)	160.5 (54)	164.7(43.5)	<0.001

Results:

1. During the follow up 31 (16%) CV events and 7 (3%) CV deaths occurred with a mean time to the event of 21±12.5 months
2. Twenty one (11%) patients started dialysis within a mean time of 20±9 months
3. With regards to baseline characteristics, patients who developed any of the 2 major end points had significant higher VCAM-1 and LVMI levels, higher proportion of DM and lower MDRD and serum albumin comparing with patients who did not experience an event. Patients who developed CV death/event had significant higher age and IL-6, whereas patients reaching ESRD had significant lower Hb, higher UPR and serum phosphorus comparing with the other two groups
4. The statistically important predictive factors for the **CV outcome** were: **DM** (RR: 0.455, 95%CI: 0.22-0.932, p=0.03), **serum albumin** (RR: 0.296, 95%CI: 0.113-0.773, p=0.013), **LVMI** (RR: 1.0, 95% CI: 1.009-1.001, p=0.021) and **VCAM-1** (RR: 1.0007 95% CI: 1.00-1.0013, p=0.026)
5. For the **renal outcome** significant factors were: **eGFR-MDRD** (RR: 0.894, 95%CI: 0.844-0.947, p<0.001) and **UPR** (RR 1.0005, 95% CI: 1.0002-1.0007, p<0.001)

Conclusions:

The predictive value of traditional risk factors resulted to be superior to that of novel risk factors with regards to CV disease and ESRD (requiring dialysis) in long term CKD 1-4 stage patients

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Lab methods / Biomarkers

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