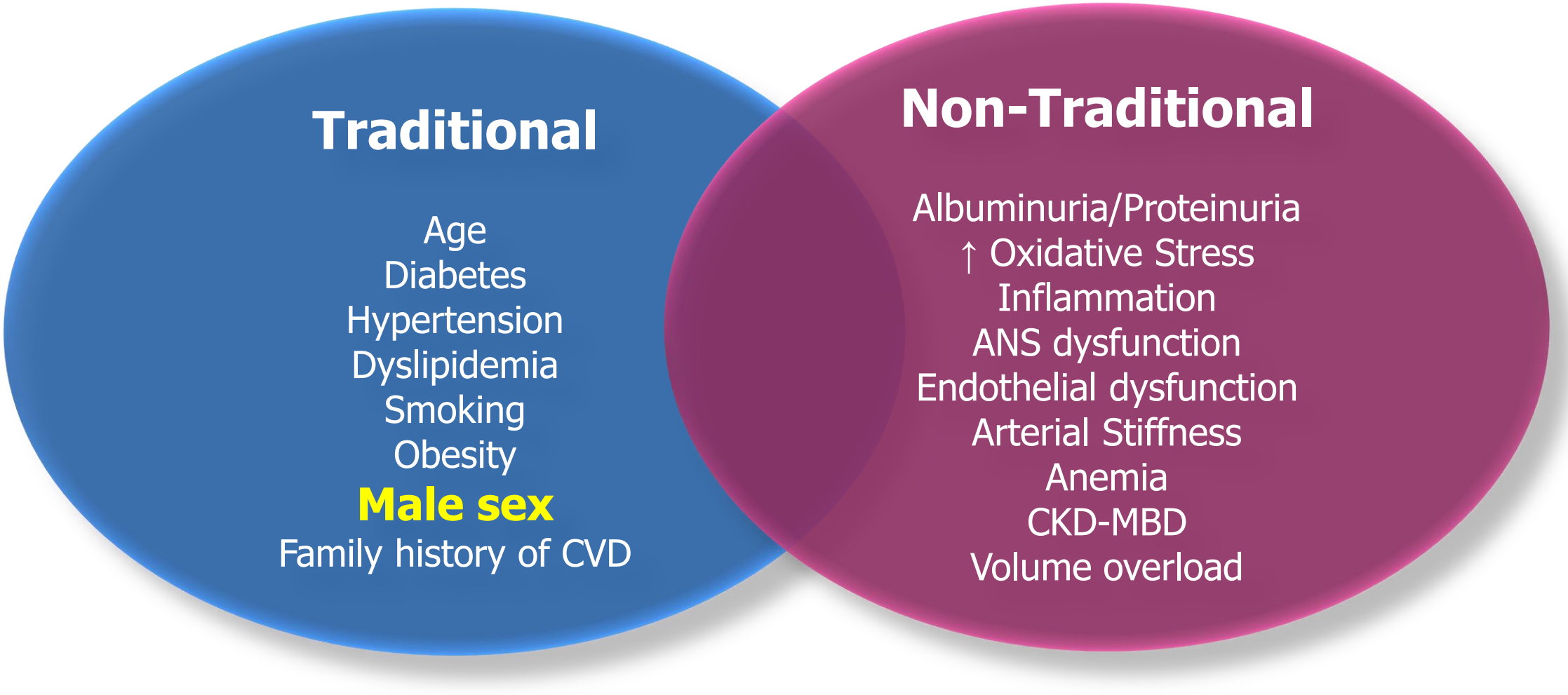
THE INFLUENCE OF AMBULATORY BP ON THE ASSOCIATIONS OF SEX WITH CARDIOVASCULAR EVENTS AND MORTALITY IN DIALYSIS PATIENTS: A PROSPECTIVE COHORT STUDY

F. IATRIDI[1], M. THEODORAKOPOULOU[1], A. KARAGIANNIDIS[1], A. GEORGIOU[1], A. KARPETAS[2], E. KARKAMANI[1], D. FAITATZIDOU[1], N. HADDAD[1], A. PAPAGIANNI[1], P. SARAFIDIS[1]

1) First Department of Nephrology, Hippokration Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; 2)Therapeutiki Hemodialysis Units, Thessaloniki, Greece

Α΄ ΝΕΦΡΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ Α.Π.Θ.
Γ.Ν.Θ. ΙΠΠΟΚΡΑΤΕΙΟ

CV risk factors in CKD



Fliser D et al. Kidney Int Suppl (2011)

Effects of sex differences in associations of BP with mortality in CKD

- 906 pre-dialysis CKD patients, f-up 10.7 years

AIMS:

- Men vs women
- Office BP
- ABP at goal (daytime BP <135/85 and nighttime BP <120/70 mmHg)
- Risk of all-cause mortality and ESKD

Table 2. Office BP, ABP and treatment in CKD patients stratified by gender

Blood pressure	Women ($N = 353$)	Men ($N = 553$)	P-value
Office systolic BP (mmHg)	145 ± 21	144 ± 19	0.30
Office diastolic BP (mmHg)	81 ± 12	82 ± 11	0.31
24-h systolic BP (mmHg)	129 ± 17	132 ± 17	0.005
24-h diastolic BP (mmHg)	73 ± 11	75 ± 10	<0.001
Daytime systolic BP (mmHg)	131 ± 16	134 ± 17	0.005
Daytime diastolic BP (mmHg)	75 ± 11	78 ± 11	<0.001
Nighttime systolic BP (mmHg)	123 ± 20	127 ± 19	0.006
Nighttime diastolic BP (mmHg)	67 ± 12	70 ± 11	<0.001
Non-dipping (%)	66.3	72.7	0.04
Antihypertensive drugs (n)	2 (1–3)	2 (1–3)	0.33
RAS inhibitors (%)	72.8	70.5	0.46

Minutolo et al. Nephrol Dial Transplant 2021

Effects of sex differences in associations of BP with mortality in CKD

In patients with **pre-dialysis** CKD, sex **difference in ABP control** significantly contributes to the **poor prognosis** of men compared with women.

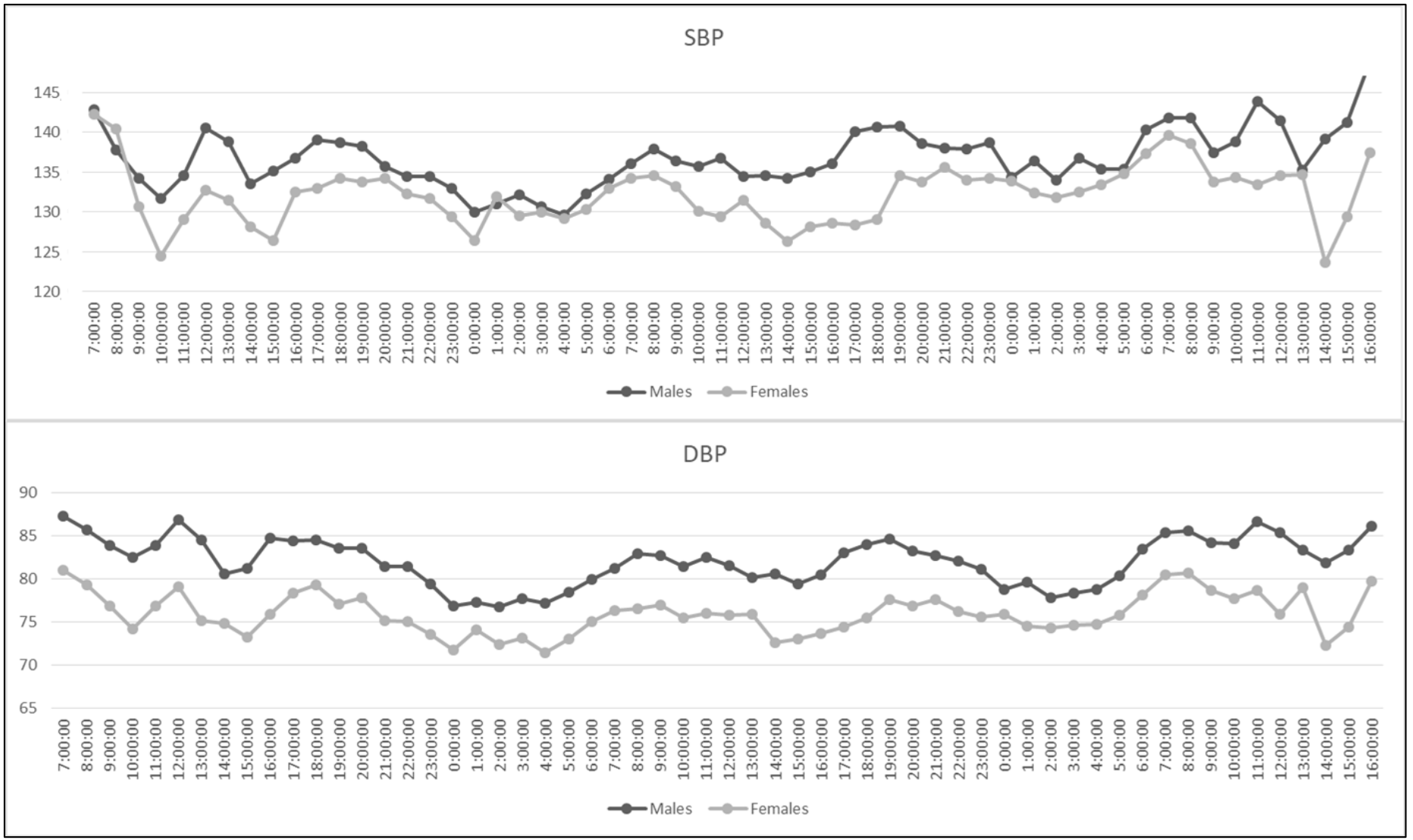
ABP and survival differences were disclosed in the absence of any difference in office BP

	Risk of event [HR (95% CI)]			
	Model 1	Model 2	Model 3	Model 4
ESKD				
Men versus women	**1.34 (1.02–1.76)**	**1.35 (1.03–1.77)**	1.29 (0.98–1.70)	1.30 (0.98–1.71)
Office BP at goal	–	1.14 (0.86–1.51)	–	1.29 (0.96–1.73)
Ambulatory BP at goal	–	–	**0.52 (0.36–0.74)**	**0.49 (0.34–0.70)**
All-cause death				
Men versus women	**1.36 (1.02–1.83)**	**1.36 (1.02–1.83)**	1.31(0.98–1.77)	1.31 (0.97–1.77)
Office BP at goal	–	1.00 (0.73–1.35)		1.09 (0.80–1.49)
Ambulatory BP at goal	–	–	**0.60 (0.44–0.81)**	**0.59 (0.43–0.80)**

Model 1 is stratified by CKD stage and center and adjusted for age, smoking, BMI, diabetes mellitus, history of cardiovascular disease, LVH, phosphate, haemoglobin, eGFR, proteinuria, number of antihypertensive drugs and use of inhibitors of RAS.
Model 2 adjusted as Model 1 + office BP at goal (≤140/90 mmHg if non-proteinuric and ≤130/80 mmHg if proteinuric).
Model 3 adjusted as Model 1 + ABP at goal (daytime <135/85 mmHg and nighttime <120/70 mmHg).
Model 4 adjusted as Model 1 + office and ABP at goal.

Minutolo et al. Nephrol Dial Transplant 2021

Sex differences in BP in hemodialysis



N=220 hemodialysis with 48h ABPM

Men vs women : ↑ ABP levels

Theodorakopoulou, et al. J Hypertens 2022

Aims

The aim of this study was to investigate **the influence of ambulatory BP** on the **associations of sex with cardiovascular events and mortality** in hemodialysis individuals

Methods

- Prospective cohort study
- 220 hemodialysis patients (129 male and 91 female)
- Mean follow-up 53.4±31.1 months

- Inclusion criteria:
  1. age >18 years,
  2. ESKD under hemodialysis for >3 months, performed with thrice-weekly standard sessions,
  3. informed written consent
- Exclusion criteria:
  1. chronic atrial fibrillation or other diagnosed arrhythmia intervening with a proper ABPM recording
  2. non-functional arteriovenous fistula in the contralateral brachial arm area of the one used for vascular access that could interfere with proper ABPM recording
  3. modification of dry weight or anti-hypertensive treatment during 1 month prior to enrolment
  4. myocardial infarction, angina pectoris and stroke during 1 month before study initiation,
  5. history of malignancy or other comorbid condition linked with poor prognosis

Methods

- **48h ambulatory BP monitoring**
  - Mobil-O-Graph (recordings every 20 min during daytime (7:00-22:59) and 30 min during nighttime (23:00-6:59)

Study end-points

- Primary end-point: cardiovascular mortality
- Secondary end-point: composite of was 1) cardiovascular death, 2) non-fatal myocardial infarction, 3) non-fatal stroke, 4) resuscitation after cardiac arrest, 5) hospitalization for heart failure, 6) coronary or peripheral revascularization procedure

Statistical analysis

- Kaplan Meier survival analysis: to assess the cumulative freedom from the primary and secondary end-points in men and women

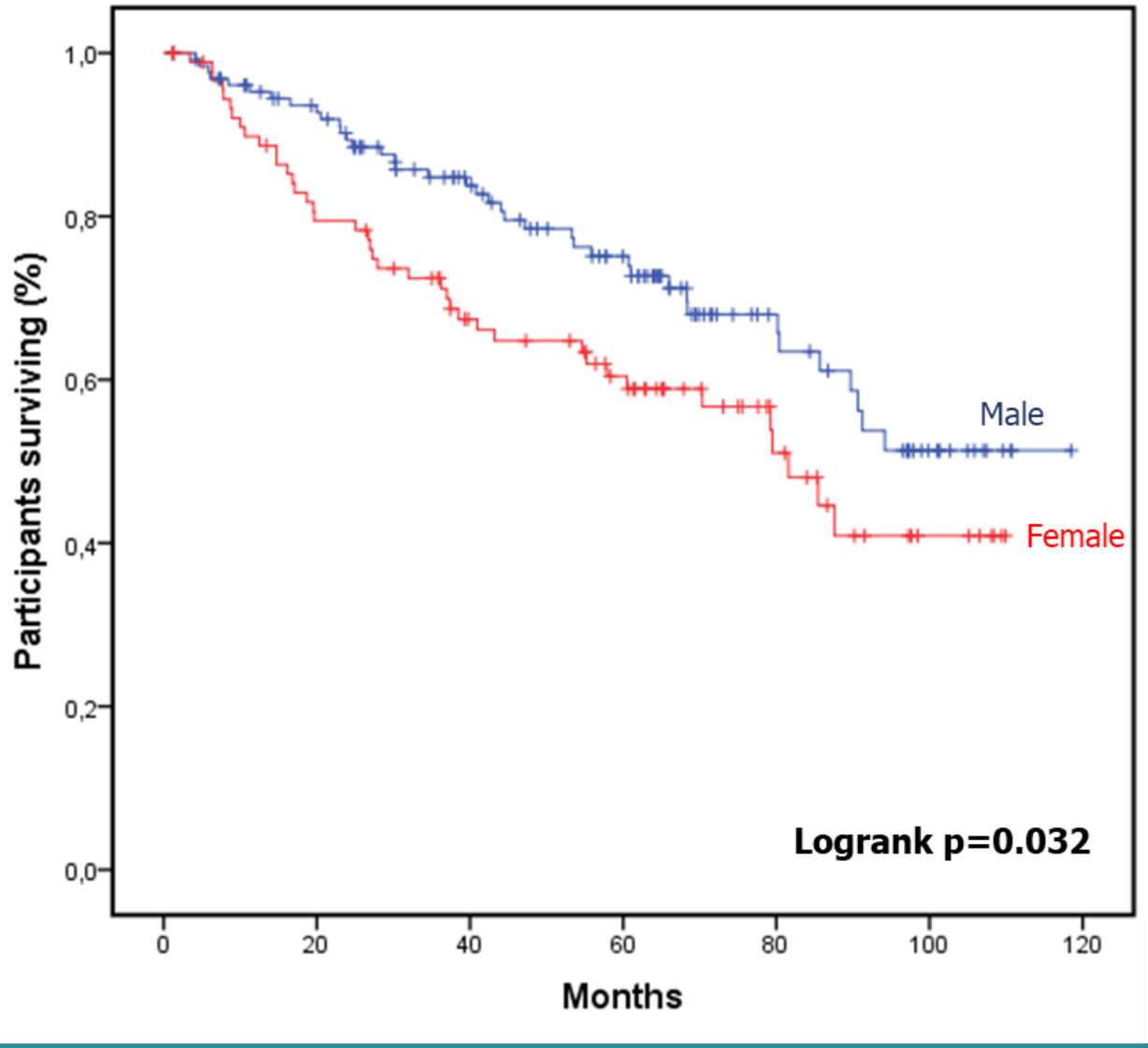
- Univariate and multivariate Cox regression analysis and calculation of crude and adjusted Hazard Ratios for the primary and the secondary end-points
  - **Men**: Reference group
  - Model 1: adjusted for age, diabetes, dialysis vintage, CAD
  - Model 2: adjusted for age, diabetes, dialysis vintage, CAD **and 44h SBP**

Baseline characteristics

Parameter	Male	Female	p-value
N	129	91	
Age (years)	63.8±13.0	65.7±13.6	0.282
Dialysis vintage (months)	27.8 (47.7)	25.0 (36.8)	0.307
BMI (kg/m^2)	25.3±5.7	24.6±6.8	0.402
Diabetes mellitus (n, %)	38 (29.5%)	32 (35.2%)	0.371
Coronary heart disease (n, %)	43 (33.3%)	17 (18.7%)	**0.016**
Peripheral arterial disease (n, %)	10 (7.8%)	7 (7.7%)	0.987
Stroke (n, %)	10 (7.8%)	8 (8.8%)	0.782
Dyslipidaemia (n, %)	33 (25.6%)	20 (22.0%)	0.538
Haemoglobin (g/dl)	11.5±1.3	11.1±1.2	**0.020**
Uric acid (mg/dl)	6.2±1.1	6.6±7.7	0.583
Urea (mg/dl)	140.4±34.2	135.6±39.2	0.333
Creatinine (mg/dl)	8.9±2.5	7.2±2.2	**<0.001**
Sodium (mg/dl)	137.8±2.9	137.2±3.6	0.131
Potassium (mg/dl)	4.9±0.6	4.8±0.7	0.505
Calcium (mg/dl)	8.9±0.7	9.1±0.7	0.165
Phosphate (mg/dl)	5.2±1.4	5.1±1.4	0.803
Parathormone (pg/mL)	267.0 (183.0)	233.0 (269.0)	0.266
Ferritin (ng/mL)	334.0 (530.8)	402.0 (647.8)	0.224

Parameter	Male	Female	p-value
ABPM			
48-hour SBP (mmHg)	137.2±17.4	132.2±19.2	**0.045**
1st 24-hour SBP (mmHg)	135.6±18.4	131.3±19.7	0.094
2nd 24-hour SBP (mmHg)	139.0±17.8	133.3±19.5	**0.025**
48-hour DBP (mmHg)	81.9 ±12.1	75.9±11.7	**<0.001**
1st 24-hour DBP (mmHg)	81.6±12.7	75.6±11.6	**<0.001**
2nd 24-hour DBP (mmHg)	82.6±12.0	76.2±12.0	**<0.001**
Antihypertensive agents			
Number of antihypertensives	1.4±1.0	1.4±1.1	0.703
ACEi/ARBs (n, %)	35 (27.1%)	19 (20.9%)	0.289
CCBs (n, %)	61 (47.3%)	42 (46.2)	0.868
MRAs (n, %)	1 (0.8%)	2 (2.2%)	0.571
β-blocker (n, %)	67 (51.9%)	45 (49.5%)	0.716
Centrally active agents (n, %)	19 (14.7%)	16 (17.6%)	0.569
Diuretics (n, %)	46 (35.7%)	31 (34.1%)	0.807

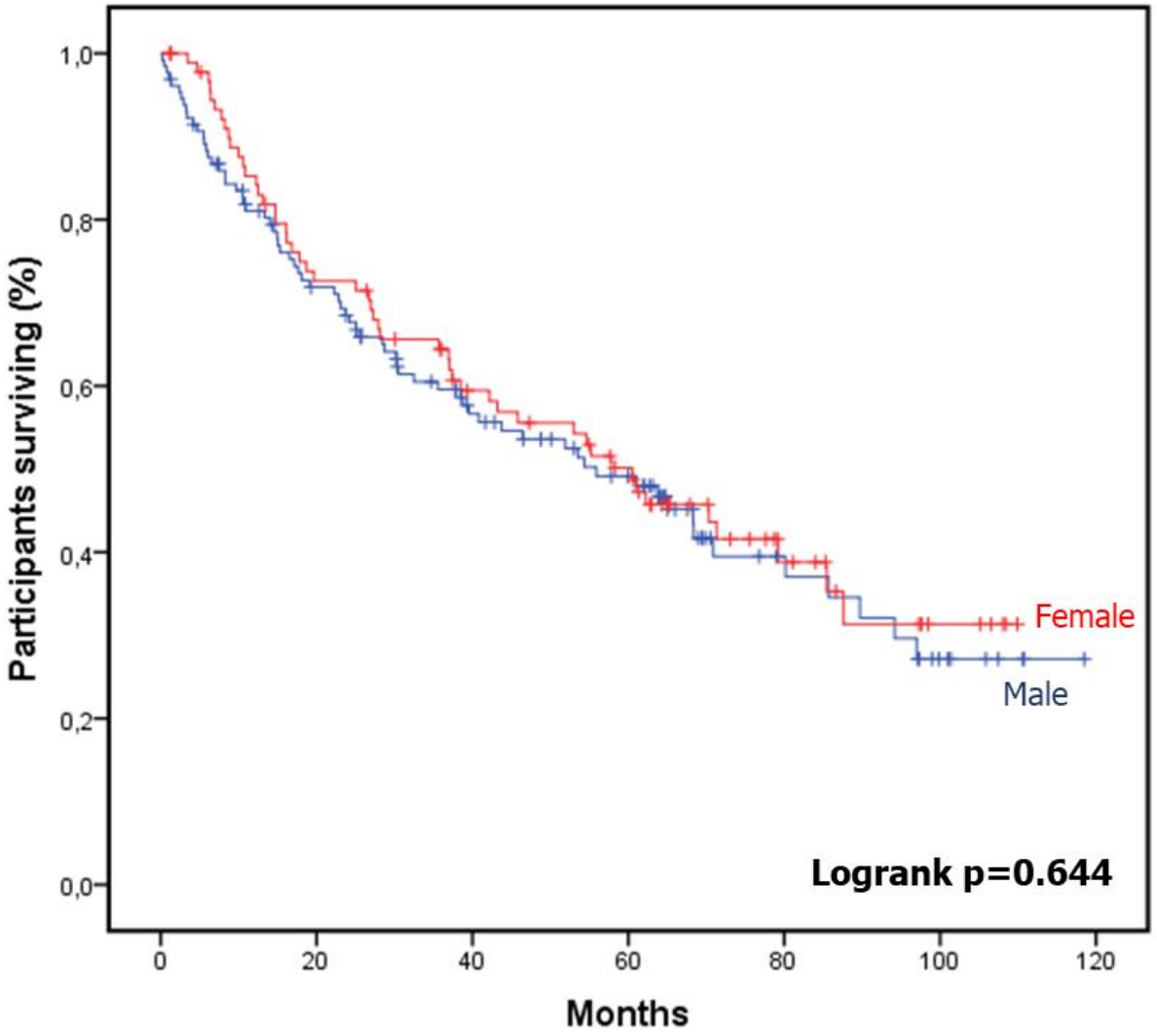
Primary end-point



Hazard Ratios

- Crude HR=1.613, 95%CI 1.037 - 2.509
- Adjusted for age, DM, dialysis vintage, CAD HR=1.464, 95%CI 0.929 - 2.307
- Adjusted for age, DM, dialysis vintage, CAD **and 44-h SBP** HR=1.498, 95%CI 0.947 - 2.368

Secondary end-point



Hazard Ratios

- Crude HR=0.918, 95%CI 0.638 - 1.320
- Adjusted for age, DM, dialysis vintage, CAD HR=0.866, 95%CI 0.596 - 1.260
- Adjusted for age, DM, dialysis vintage, CAD **and 44-h SBP** HR=0.911, 95%CI 0.625 - 1.327

Strengths and limitations

- ✓ The first study that investigated the influence of ambulatory BP on the associations of sex with cardiovascular events and mortality in hemodialysis individuals
- ✓ 48h ABPM
- ✓ Large sample size (220 patients) and long follow-up (~4,5 years)

- – Baseline evaluation only once
- – Caucasian race

Conclusions

- Ambulatory BP levels are higher in male than female hemodialysis patients

- In contrast to patients with pre-dialysis CKD, ambulatory BP does not appear to significantly influence the relationship between sex and adverse cardiovascular outcomes in hemodialysis patients.

- Cardiovascular mortality is extremely high in patients with ESKD and is affected by both general and CKD-related risk factors, and consequently there is no protection associated with the presence of female sex

Thank you very much for your attention!