# PROGNOSIS OF WHITE COAT HYPERTENSION AND MASKED HYPERTENSION IN NON-DIALYSIS CKD PATIENTS

*Roberto Minutolo [1], Francis B. Gabbai [2] , Rajiv Agarwal [3], Paolo Chiodini MSc [4], Silvio Borrelli [1], Giovanna Stanzione [1], Felice Nappi [5], Vincenzo Bellizzi [6], Giuseppe Conte [1], Luca De Nicola [1]*

[1] Division of Nephrology, Second University of Naples, Italy, [2] Dept. of Medicine, University of California at San Diego, U.S.A., [3] Division of Nephrology, Indiana University, Indianapolis, U.S.A., [4] Dept. of Medicine and Public Health, Second University of Naples, Italy, [5] Nephrology, University Hospital, Salerno, Italy, [1] Nephrology, County Hospital, Nola, Italy

## BACKGROUND AND AIM

- 24h ambulatory blood pressure (ABP) monitoring, together with clinic blood pressure (CBP), allows to identify patients with altered BP profiles: white coat (WCH), masked hypertension (MH) and sustained hypertension (SH).
- In CKD patients, prevalence of WCH and MH varies across studies and differs from that reported in essential hypertension.
- At variance with essential hypertension, in CKD there is no available information on the independent prognostic role of WCH/ MH.
- **This multicenter prospective cohort study was aimed at evaluating the impact of WCH, MH and SH on CV and renal prognosis.**

## METHODS

**INCLUSION CRITERIA**

- Consecutive adult patients with CKD stage 2-5, attending three Nephrology clinics from ≥ 6 months with at least 2 visits during 2003-2006.
- Hypertension (CBP≥130/80 mmHg or antihypertensive treatment).

**EXCLUSION CRITERIA**

- Dialysis/transplant,
- eGFR changes >30% in the previous 3 months,
- change of therapy 2 weeks prior to enrollment,
- atrial fibrillation
- inadequate ABP (<14/<7 readings during the day/night).

**ABP MONITORING** (Spacelabs 90207)

- BP was recorded every 15 min (7:00-23:00) and every 30 min (23:00-7:00). Daytime and nighttime periods were derived from the patient's diary. ABP was always obtained on a workday and under regular antihypertensive treatment.

**PATIENTS' CLASSIFICATION**

- Patients were at goal for ABP when daytime was <135/85 and nighttime <120/70 mmHg [1], and at goal for CBP if <130/80 mmHg [2]. Based on these cut-offs, patients were classified as follows:
  - **Treated normotensive, t-NOR (CBP and ABP at goal),**
  - **White coat hypertension, WCH (CBP above goal and ABP at goal)**
  - **Masked hypertension, MH (CBP at goal and ABP above goal)**
  - **Sustained hypertension, SH (CBP and ABP above goal).**

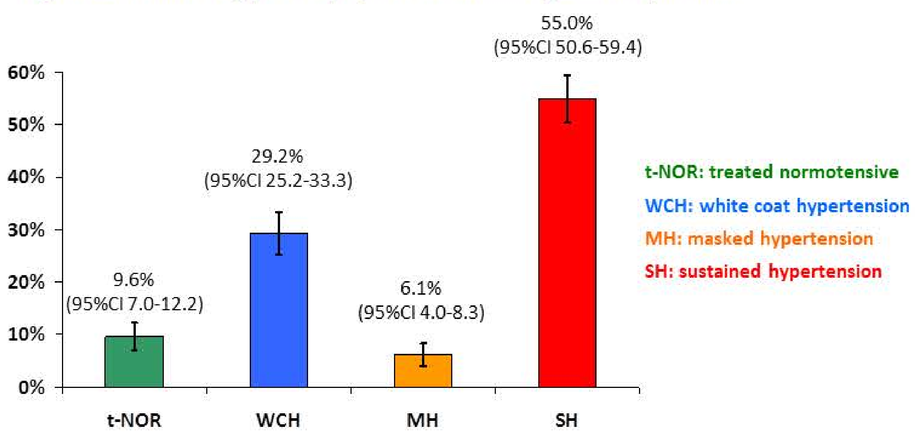
**ENDPOINTS**

- Primary: composite endpoint of fatal and non-fatal CV events and composite endpoint of renal death (ESRD or death)
- Secondary: single components of renal death, that, is, ESRD and all-cause mortality.

Patients were followed until 10/31/2013, death or ESRD and censored on the date they had the last clinic visit.

## RESULTS

***Figure 1.*** *Prevalence of pressor profiles in the cohort of 489 CKD patients.*




### SURVIVAL ANALYSIS

- Patients were followed for up to 9 years (median 5.2, IQR 3.1-7.1 years).
- **Renal death occurred in 214 patients**
  - 111 progressed to ESRD
  - 103 died.
- **CV outcome occurred in 131 patients** (67 non-fatal CV events and 82 CV deaths, 18 of which occurred after a first non-fatal CV event).
  - 84 acute myocardial infarctions (54 fatal)
  - 30 strokes (17 fatal)
  - 17 acute heart failures (8 fatal)
  - 18 peripheral vascular accidents (3 fatal)

***Figure 2****. Incidence of renal death and fatal and non-fatal CV event (competing-risk)*

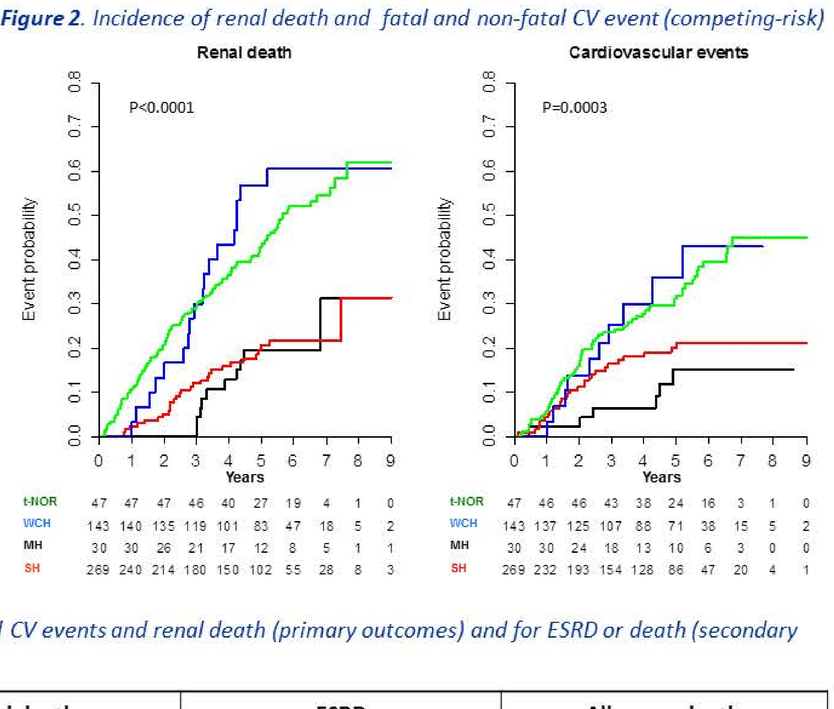



***TABLE 1****: Demographic, clinical and therapeutic characteristics of patients*

| | t-NOR (N=47) | WCH (N=143) | MH (N=30) | SH (N=269) | P |
|---|---|---|---|---|---|
| Age (years) | 62.9±13.6 | 64.6±13.5 | 60.7±18.9 | 64.9±14.0 | 0.4 |
| Male gender (%) | 53.2 | 51.0 | 60.0 | 64.7 | 0.05 |
| Diabetes (%) | 29.8 | 30.8 | 30.0 | 40.5 | 0.1 |
| Active smoking (%) | 14.9 | 18.9 | 33.3 | 25.7 | 0.1 |
| BMI (kg/m$^2$) | 27.9±5.6 | 29.2±5.1 | 27.6±4.9 | 29.0±5.3 | 0.3 |
| Prior CV disease (%) | 23.4 | 27.3 | 26.7 | 33.5 | 0.4 |
| Renal disease (%) | | | | | 0.004 |
| *Hypertension* | 44.7 | 53.8 | 26.7 | 41.6 | |
| *Diabetic Nephropathy* | 6.4 | 16.8 | 16.7 | 23.4 | |
| *Glomerulonephritis* | 19.1 | 7.7 | 13.3 | 7.8 | |
| *APKD* | 4.3 | 1.4 | 13.3 | 6.3 | |
| *Other/Unknown* | 25.5 | 20.3 | 30.0 | 20.8 | |
| eGFR (mL/min/1.73m$^2$) | 43.2±17.5 | 47.6±17.1 | 41.4±16.5 | 41.2±21.6 | 0.02 |
| Hemoglobin (g/dL) | 13.3±1.8 | 13.0±1.7 | 12.9±1.6 | 12.8±1.9 | 0.4 |
| Cholesterol (mg/dL) | 186±35 | 191±38 | 194±36 | 189±38 | 0.8 |
| Proteinuria (g/day) | 0.2 [0.1-0.8] | 0.2 [0.1-0.4] | 0.3 [0.1-0.7] | 0.4 [0.1-1.7] | <0.001 |
| UNaV (mEq/day) | 131±49 | 152±60 | 139±79 | 157±64 | 0.05 |
| Clinic BP (mmHg) | 119±8/70±8 | 147±14/83±10 | 118±8/70±7 | 153±17*/85±11 | - |
| 24h BP (mmHg) | 109±8/66±7 | 115±8#/66±7 | 126±9/72±8 | 139±14†/77±10† | - |
| Daytime BP (mmHg) | 112±9/68±8 | 118±9#/70±8 | 127±10/74±8 | 142±15†/80±11† | - |
| Nighttime BP (mmHg) | 103±8/59±6 | 106±8/59±6 | 121±10/68±8 | 133±18†/71±10 | - |
| Non dippers (%) | 66.0 | 48.3 | 76.7 | 67.7 | <0.001 |
| BP lowering drugs (n) | 2 [1-3] | 2 [2-3] | 2 [1-3] | 3 [2-4] | 0.01 |
| Receiving therapy (%) | 100 | 91.6 | 100 | 92.2 | 0.003 |
| CEI and/or ARB (%) | 87.2 | 83.9 | 53.3 | 81.0 | 0.001 |
| Diuretics (%) | 46.8 | 53.1 | 40.0 | 54.9 | 0.4 |
| Calcium blockers (%) | 38.3 | 35.0 | 46.7 | 49.8 | 0.03 |
| Beta-Blockers (%) | 31.9 | 35.7 | 30.0 | 36.1 | 0.9 |
| Other classes (%) | 8.5 | 13.3 | 3.3 | 23.4 | 0.002 |

Data are mean±SD, median [IQR] or percentage. APKD, Autosomal Polycystic Kidney Disease; eGFR, estimated GFR by the 4-variable MDRD equation; UNaV, urinary sodium excretion; BP, blood pressure; Non dippers: night/day ratio of systolic ambulatory BP ≥0.9.
* P<0.05 vs WCH; # P<0.05 vs t-NOR; † P<0.05 vs MH.

***TABLE 2****. Cox regression analysis estimating the risk for fatal and non-fatal CV events and renal death (primary outcomes) and for ESRD or death (secondary outcomes) associated to the different BP profiles*

| | Fatal and non-fatal CV events | | Renal death | | ESRD | | All-cause death | |
|---|---|---|---|---|---|---|---|---|
| | Events (event rate)* | HR (95%CI)[a] | Events (event rate)* | HR (95%CI)[a] | Events (event rate)* | HR (95%CI)[a] | Events (event rate)* | HR (95%CI)[a] |
| **Treated normotensive** | 6 (2.19) | Reference | 14 (4.83) | Reference | 7 (2.41) | Reference | 7 (2.41) | Reference |
| **White coat hypertension** | 29 (3.95) | 1.73 (0.71-4.20) | 31 (3.86) | 1.41 (0.72-2.75) | 11 (1.37) | 1.86 (0.65-5.30) | 20 (2.49) | 1.13 (0.46-2.75) |
| **Masked hypertension** | 10 (7.95) | **4.44 (1.57-12.6)** | 19 (13.18) | **4.94 (2.36-10.4)** | 9 (6.24) | **5.94 (1.93-18.3)** | 10 (6.93) | **3.68 (1.32-10.3)** |
| **Sustained hypertension** | 86 (7.99) | **3.31 (1.43-7.67)** | 150 (12.30) | **3.36 (1.86-6.05)** | 84 (6.89) | **5.65 (2.36-13.5)** | 66 (5.41) | **2.31 (1.02-5.24)** |

* Event rate expressed as event per 100 patient-year). [a] Model is adjusted for age, gender, BMI, diabetes, history of CV disease, hemoglobin, eGFR, 24h Proteinuria, non dipping status, use of CEI/ARB and stratified for Center.

***TABLE 3****. Cox regression analysis estimating the risk for fatal and non-fatal CV events and renal death (primary outcomes) and for ESRD or death (secondary outcomes) in the four groups defined using four different cut-off values for clinic blood pressure (CBP) and ambulatory blood pressure (ABP).*

| | Spanish Registry [3] | | | AASK Study [4] | | | CKD-JAC [5] | | | Veterans cohort [6] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Cut-off CBP | <140/90 mmHg | | | <140/90 mmHg | | | ≤140/90 mmHg | | | Systolic<130 mmHg | | |
| Cut-off ABP | 24h<130/80 mmHg | | | day<135/85 and night <120/70 | | | 24h≤130/80 mmHg | | | 24h systolic<130 mmHg | | |
| **CV events** | % | Events | HR (95%CI) | % | Events | HR (95%CI) | % | Events | HR (95%CI) | % | Events | HR (95%CI) |
| **Treated normotensive** | 20.9 | 16 | Ref. | 16.8 | 12 | Ref. | 27.0 | 23 | Ref. | 17.6 | 13 | Ref. |
| **White coat hypertension** | 28.8 | 35 | 1.53 (0.83-2.82) | 22.1 | 23 | 1.55 (0.70-2.35) | 26.0 | 30 | 1.33 (0.76-2.32) | 39.3 | 40 | 1.48 (0.71-3.08) |
| **Masked hypertension** | 10.4 | 15 | **3.00 (1.39-6.19)** | 14.5 | 19 | **3.16 (1.50-6.68)** | 12.1 | 18 | **2.34 (1.24-4.40)** | 2.9 | 6 | **3.37 (1.21-9.34)** |
| **Sustained hypertension** | 39.9 | 65 | **2.47 (1.34-4.43)** | 46.6 | 77 | **2.68 (1.46-4.90)** | 34.9 | 60 | **2.26 (1.36-3.74)** | 40.3 | 72 | **2.47 (1.21-5.01)** |
| **Renal death** | | | | | | | | | | | | |
| **Treated normotensive** | 20.9 | 34 | Ref. | 16.8 | 22 | Ref. | 27.0 | 46 | Ref. | 17.6 | 28 | Ref. |
| **White coat hypertension** | 28.8 | 43 | 1.40 (0.87-2.24) | 22.1 | 23 | 1.26 (0.68-2.31) | 26.0 | 40 | 1.25 (0.80-1.95) | 39.3 | 59 | 1.18 (0.67-2.06) |
| **Masked hypertension** | 10.4 | 25 | **2.36 (1.35-4.12)** | 14.5 | 37 | **3.63 (2.07-6.34)** | 12.1 | 30 | **2.09 (1.28-3.44)** | 2.9 | 11 | **2.53 (1.21-5.27)** |
| **Sustained hypertension** | 39.9 | 112 | **1.95 (1.29-2.95)** | 46.6 | 132 | **2.99 (1.85-4.85)** | 34.9 | 98 | **1.61 (1.10-2.36)** | 40.3 | 116 | **2.19 (1.32-3.62)** |

% indicates percent of patients in each group. Cox models are adjusted for age, gender, BMI, diabetes, history of CV disease, hemoglobin, eGFR, 24h Proteinuria, non dipping status, use of CEI/ARB and stratified for Center.

## CONCLUSIONS

In non-dialysis CKD patients regularly followed in Italian renal clinics:

- WCH is condition carrying a relatively low risk, whereas MH is associated with a high cardio-renal risk which is not dissimilar from that observed in patients with SH.
- These results were consistent across different definitions of BP profiles.
- **These findings support the use of ABP monitoring in all hypertensive CKD patients to better stratify their cardio-renal risk and, likely, to optimize the treatment.**

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51ERA-EDTA
160-MP
H) Clinical Nephrology, CKD. H1) Lab methods, progression & risk factors for CKD 1-5, nutrition in CKD, renal diseases (except GNs and cystic diseases).
Roberto Minutolo
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