

SUPPLEMENTARY DATA

Title: Prognostic Importance of Resistant Hypertension in Patients with Type 2 Diabetes: The Rio de Janeiro Type 2 Diabetes Cohort Study.

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Content: Supplemental Table S1 and Figure S1.

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Supplementary Table S1. Baseline characteristics and endpoints incidence of diabetic patients divided according to the presence or absence of apparent resistant hypertension and of white-coat (controlled) and true (uncontrolled) resistant hypertension, defined according to the 2017 ACC/AHA criteria (office BP $\geq 130/80$ mmHg and ambulatory 24-hour BP $\geq 125/75$ mmHg, respectively).

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Characteristics	Non-apparent RHT (n=323)	Apparent RHT (n=323)	White-coat controlled RHT (n=99)	True uncontrolled RHT (n=234)
Age (years)	58.7 (10.1)	61.7 (8.5) *	63.0 (7.6) *	61.2 (8.8) †
Male sex (%)	43.7	33.4 †	29.3 †	35.0 ‡
Body mass index (kg/m ²)	28.8 (4.8)	30.7 (4.7) *	30.5 (4.8) †	30.6 (4.7) *
Smoking, current/past (%)	48.1	40.7	40.4	40.8
Physical activity (% active)	24.1	20.5	18.2	21.0
Diabetes duration (years)	7 (2.5-15)	9 (4-16) †	10 (5-18.5) *	8 (4-15)
Chronic diabetic complications (%)				
Cerebrovascular disease	5.9	13.3 †	10.1	15.0 *
Coronary artery disease	9.9	22.0 *	21.2 †	21.8 *
Peripheral artery disease	13.0	21.1 †	19.4	21.8 †
Retinopathy	28.9	35.7	39.8 ‡	34.6
Nephropathy	23.8	38.9 *	27.8	41.8 *
Peripheral neuropathy	26.6	31.5	28.6	31.8

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Diabetes treatment (%)				
Metformin	88.2	87.3	82.8	89.3
Sulfonylureas	44.3	43.3	44.4	43.2
Insulin	43.7	52.9 ‡	49.5	54.3 ‡
Aspirin	87.9	94.9 †	94.9 ‡	93.9 ‡
Dyslipidemia (%)				
Statins use (%)	73.1	82.6 †	81.8	83.2 †
Blood pressures (mmHg)				
Office SBP	133 (18)	158 (25) *	151 (23) *	160 (26) *
Office DBP	78 (11)	86 (14) *	83 (14) *	86 (14) *
Ambulatory 24h SBP	124 (12)	133 (17) *	116 (6) *	140 (14) *
Ambulatory 24h DBP	73 (9)	75 (11) ‡	65 (6) *	79 (10) *
Number of anti-hypertensive drugs	1 (1-2)	3 (3-4) *	3 (3-4) *	3 (3-4) *
Laboratory variables				
Fasting glycemia (mmol/l)	7.9 (2.7)	8.4 (2.8) ‡	7.8 (2.6)	8.6 (2.9) *
HbA _{1c} (%)	7.5 (1.4)	7.9 (1.6) *	7.4 (1.3)	8.1 (1.7) *
(mmol/mol)	60 (15.3)	63 (17.5)	57 (14.2)	65 (18.6)
Triacylglycerol (mmol/l)	1.8 (1.2)	2.0 (1.8)	1.9 (1.9)	2.1 (1.7) †
HDL-cholesterol (mmol/l)	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)
LDL-cholesterol (mmol/l)	2.8 (0.8)	2.8 (0.9)	2.6 (0.8)	2.9 (0.9)
Glomerular filtration rate (ml/min/1.73m ²)	86 (19)	76 (20) *	77 (20) *	76 (20) *
Albuminuria (mg/24h)	12 (7-26)	17 (7-66) †	10 (6-32)	19 (8-104) *

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Outcomes §

Total CVEs	66 (21.8)	111 (42.2) *	29 (33.6)	84 (45.3) *
MACE	53 (17.0)	92 (33.4) *	23 (25.4)	71 (36.6) *
Cardiovascular mortality	31 (9.6)	70 (24.3) *	19 (20.3) †	52 (25.6) *
All-cause mortality	85 (26.3)	137 (47.5) *	39 (41.7) †	101 (49.7) *
Renal composite	93 (34.0)	107 (44.2)	26 (32.3)	82 (48.5) ‡
Retinopathy				
(incident/worsening) (n=526)	79 (49.5)	77 (53.0)	28 (61.3)	49 (47.4)
Peripheral neuropathy				
(incident/ worsening) (n=510)	81 (30.6%)	93 (38.0%)	25 (30.9%)	59 (43.7%) ‡

Values are proportions, and means (standard deviations) or medians (interquartile range).

* p<0.001; † p<0.01; ‡ p<0.05 for bivariate comparisons with the non-apparent RHT subgroup.

§ Values are absolute numbers (incidence rate per 1000 patient-years of follow-up), except for peripheral neuropathy that are absolute numbers (proportions).

Abbreviations: RHT, resistant hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; CVEs, cardiovascular events; MACE, major adverse cardiovascular events.

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Supplementary Figure S1. Kaplan-Meier estimation curves of cumulative events incidence during follow-up for major adverse cardiovascular events (MACE) outcome (panels A and B), for cardiovascular mortality (panels C and D), for all-cause mortality (panels E and F) and for the renal composite outcome (panels G and H), in patients classified as non-resistant hypertension (non-RHT), white-coat/controlled resistant hypertension (wc-RHT), and true uncontrolled resistant hypertension (true RHT) by 24-hour ambulatory BP levels defined by the traditional cut-off value ($\geq 130/80$ mmHg, left panels A, C, E and G) and by the new 2017 ACC/AHA cut-off value ($\geq 125/75$ mmHg, right panels B, D, F and H).

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