

A study of Factors AssoCiated with Treatment Resistant HYpertension (FACT-RHY): a description of phenotypical, physiological and biochemical characteristics of patients with true treatment-resistant hypertension compared to treated patients with hypertension.

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Introduction:

Treatment-resistant hypertension (TRH) is present in around 10% of the patients with treated hypertension. Its prevalence is often overestimated, a consequence of failure to exclude non-adherence and white-coat hypertension. We aim to describe phenotypical, biochemical and physiological characteristics of TRH in the first 100 patients recruited to FACT-RHY study (a study of Factors AssoCiated with Treatment-Resistant HYpertension).

Methods:

Patients aged 18–80 years with treated hypertension and without any confirmed causes of secondary or white-coat hypertension were eligible. All patients gave written consent and a detailed clinical history, examination, biochemical and physiological testing was performed. Clinic BP was performed in a similar method to SPRINT study¹, with the patient sat in a quiet room and an average of 5 readings was taken using BpTRU. Aortic stiffness as quantified by carotid-to-femoral pulse wave velocity (cfPWV) was measured using a Vicorder. Endothelial dysfunction was assessed by measuring levels of vascular biomarkers and reactive hyperaemia index using peripheral arterial tone. Fluid excess and body composition were assessed using bioimpedance spectroscopy. Patients with uncontrolled BP (average BpTRU >140/90mmHg) taking ≥ 3 antihypertensives or if BP controlled on ≥ 4 agents were defined as having TRH only if ≥ 3 antihypertensives were detectable by urine antihypertensive assay. All other patients were defined as a control group.

Results:

Forty-one patients had TRH, 53 were females and 51 Caucasians. Patients with TRH were older, had significantly higher waist-hip and waist-height ratios, a longer duration of hypertension and, higher prevalence of left ventricular hypertrophy and diabetes mellitus compared to controls. Patients with TRH were prescribed a higher number of antihypertensives and other medications including diuretics and lipid-lowering therapy. Biochemical testing showed that a lower estimated glomerular filtration rate and serum album and a higher kappa-lambda ratio, NT-proBNP, high-sensitivity Troponin I and aldosterone-renin ratio were associated with TRH. There were no differences in urinary albuminuria, 24-hour urinary catecholeamines and metadrenalines and daily salt intake estimated from 24-hour urinary sodium excretion. The 10-year Qrisk2 was significantly higher at 21.0% in TRH compared to 7.6% in controls ($p < 0.001$).

Parameters of arterial stiffness, cfPWV, central and peripheral pulse pressures were found to be significantly higher in patients with TRH. The cfPWV strongly correlated with increasing age ($r = 0.527$, $p < 0.001$). A higher proportion of patients were underhydrated with TRH. Forty-three patients underwent peripheral arterial tone assessment and there was no significance difference in the reactive hyperaemia index in the two

groups. Levels of endothelin-1 and vascular cell adhesion molecule 1 (VCAM-1) were found to be significantly higher in patients with TRH suggesting evidence of endothelial dysfunction. The main results of the FACT-RHY study are summarised in table 1.

Conclusions:

FACT-RHY is the first study to describe a detailed phenotype of patients with true TRH and we have shown that numerous factors are associated with TRH including a longer duration of hypertension, arterial stiffness, hyperaldosteronism, biomarkers of endothelial dysfunction and cardiac disease. A higher prevalence of target-organ damage may be responsible for a higher future risk of cardiovascular and cerebrovascular disease.