with CKD-EPI >=60 ml/min/1.73 m2 and achievement BP had low blood cortisol level (47.8±3.4) mkg/dl vs patients not achievement BP (163.7±7.8) mkg/dl (p<0.05). Aldosterone blood level was similar in both group 26.7 ng/dl vs 28.1 ng/dl respectively. Patients with CKD-EPI < 60 ml/min/1.73 m2 and achievement BP had low blood renin (34.1±3.6) ng/l as patients not achievement BP (26.8±2.5) ng/l (p>0.05). Patients with CKD-EPI < 60 ml/min/1.73 m2 and achievement BP had low blood cortisol (6.0±0.6) mkg/dl vs patients not achievement BP (127.7±8.6) mkg/dl (p<0.05).

Conclusions: In patients with RH and CKD-EPI < 60 ml/min/1.73 m2 factors related with not achievement target BP was higher blood cortisol. In patients with RH and CKD-EPI >=60 ml/min/1.73 m2 factors related with not achievement target BP was low blood renin level and higher blood cortisol.

THE RELATIONSHIP BETWEEN RESISTANT HYPERTENSION AND RENAL PROGNOSIS IN THE IN PATIENTS WITH CARDIOVASCULAR DISEASES AND CHRONIC KIDNEY DISEASE

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Objective: In the patients having chronic kidney disease (CKD) and cardiovascular diseases (CVD), the control of the blood pressure (BP) is important to prevent complications and renal function aggravation. Treatment-resistant hypertension (RHT) is hypertension not to fall to suitable BP with the antihypertensive medications more than three. Therefore, in the inpatients, we examined a ratio of RHT and renal prognosis.

Design and method: 417 inpatients (274 men, 143 women, average age 73 ± 11 years old) having CKD and CVD were examined. We investigated BP, blood test, urinalysis and oral medicines at the admission and the discharge.

Results: The ratio of RHT was 24.5 % at the admission, and 19.9 % at the discharge. We classified the patients into five groups using BP at the admission. A group (normal BP, n= 21): SBP<130mmHg and DBP<80mmHg without medications. B group (untreated hypertension, n=46): SBP more than 130mmHg or DBP more than 80mmHg without medications. C group (controlled hypertension, n=138): SBP<130 mmHg and DBP<80 mmHg with medications (one to three drugs). D group (uncontrolled hypertension, n=110): SBP more than 130 mmHg or DBP more than 80 mmHg with medications (one or two drugs). RHT group (n=102): SBP more than 130mmHg or DBP more than 80 mmHg with medications (more than three drugs). The blood pressure at admission was 128±22/76±15, 133±22/84±16, 129±23/71±15, 141±25/77±19 and 146±29/72±16, respectively. The number of the antihypertensive medications was 1.8±1.1 (C group), 1.6±1.1 (D group) and 3.1±1.2 (RHT group). In the RHT group, eGFR and the hemoglobin level were significantly lower, and the complications (diabetes, hyperuricemia, angina, atherosclerosis of lower limbs) were frequent. The factors that participated in RHT at admission were eGFR, diabetes and dyslipidemia. eGFR at the admission have related to the renal function aggravation at the discharge.

Conclusions: In the inpatients having CKD and CVD, RHT existed frequently. The factors concerning with RHT were the renal function and the aggregation of the lifestyle-relate diseases.

LEFT VENTRICULAR HYPERTROPHY REGRESSION DURING ANTIHYPERTENSIVE TREATMENT IN RESISTANT HYPERTENSION PATIENTS

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Objective: Objective: to determine the predictors of regression of left ventricular hypertrophy (LVH) in treated resistant hypertensive (RH) patients after 2.1±0.1 years of follow-up.

Design and method: We studied 51 patients with RH confirmed by the office and ambulatory blood pressure (BP) monitoring despite the use of 3 antihypertensive medications for at least 3 months. During 2 years-period patients had been treated to 12-week rotations of oral daily treatment with spironolactone, nebivolol, torsemide, eplerenone, moxonidine in addition to their baseline triple-combination. Then participants continued to receive the personal most effective fourth-line agent. Patients were divided into 2 groups: 17 patients had LV mass index (LVMI) which was increased or stayed stable after 2 years (1st group), 34 patients with a reduction of LVMI in 2 years (2nd group).

Results: Initially there were no significant differences in sex, duration of hypertension, body mass index, office and average 24-h ambulatory BP between the 2 groups. Compared with the 1st group patients from the 2nd group had a higher prevalence of non-dippers (24.3 vs 65 %, P < 0.001, respectively) and larger baseline LVMI (127.3 ± 4.1 vs 147.8 ± 6.5 g/m², P < 0.01, respectively). Patients with persistent LVH included more subjects with coronary artery disease, chronic kidney disease and had less baseline active renin concentration (all P < 0.05). After 2 years in both groups office and average 24-h BP levels have been reduced, but goal rates were achieved at 28.6 % patients of the 1st group and 44.1 % patients of the 2nd group (P < 0.05). Reduction in nighttime BP was greater in the 2nd group. Initial higher LVMI (β = 0.655; P < 0.0001), baseline 24-h urinary albumin excretion (β = - 0.475; P < 0.0001), active renin concentration (β = 0.442; P = 0.005) were predictors of δ LVMI in multivariate modeling.

Conclusions: Regression of LVH is possible in patients with RH in case of BP control, especially at night. Baseline higher LVMI, an increase of active renin concentration, decline of urinary albumin excretion are factors that determine reversibility LVH.

PREVALENCE OF SECONDARY HYPERTENSION IN PATIENTS WITH RESISTANT ARTERIAL HYPERTENSION

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Objective: Resistant hypertension is defined as blood pressure that remains above therapeutic goal despite concurrent use of three antihypertensive agents (at full or maximum tolerated doses) of different classes, one of which is a diuretic. The prevalence of secondary hypertension among patients with resistant hypertension is not exactly known.

Design and method: We retrospectively analysed the hospital records of patients with resistant arterial hypertension, who underwent complete laboratory and imaging examinations to exclude the secondary etiology of arterial hypertension. Standard descriptive statistics, Mann-Whitney U test and Fisher's exact test were used for statistical evaluation.

Results: Among the 432 patients with resistant hypertension, secondary etiology of hypertension was found in 135 (31.1%). The most frequent cause was primary aldosteronism in 85 cases (63% relatively), followed by renovascular hypertension (21 cases, 15.6%), renal parenchymal hypertension (20 cases, 14.8%). Less common causes were hyperreninism (3.7%), hypercortisolism (1.5%), pheochromocytoma (0.7%) and adrenogenital syndrome (0.7%). Obstructive sleep apnoea has been found in 63 (14.7%) patients. Patients with secondary hypertension were more frequently male (70.4% vs. 52.2%, p <0.001), had a higher left ventricular mass index (LVMI 119 vs. 106 g / m2, P = 0.037) and lower estimated glomerular filtration rate (69 vs. 75 ml/min/1.73m2, P = 0.009). Both groups did not differ in age, office blood pressure or albuminuria.

Conclusions: Secondary etiology was much more frequent (31%) in our group of patients with resistant hypertension than in non-selected hypertensive population (5-15%). Patients with secondary hypertension had more advanced target organ damage.

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IMPACT OF POLYPHARMACY AND COMORBIDITIES TO CLINICAL OUTCOMES IN RESISTANT HYPERTENSION RENAL DENERVATION GROUP

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Objective: To analyse impact of polypharmacy to blood pressure control in resistant hypertension renal denervation group.

Design and method: This prospective study included 73 selected patients with resistant hypertension and RDN (Sympathetic Renal Denervation) performed. Routine follow up was performed subsequently 1, 3, 6, 12, 24 and 48 months after the RDN. Total numbers of pills, prescibed for all diseases was registered. Two groups of patients were defined: A group- patient whom less than 7 pills prescribed and group B -more than 7 pills. Number of antihypertensive medications was analysed separately Also various characteristics were registered: age, sex, comorbidities, 24h-ABPM, arterial stiffness etc. Statistical analysis was performed using SPSS 23.0 Statistical Software.

Results: A total cases of 73 patients were included. 6 patients died, 18 failed to remain in the follow up during 4 years. Remaining 49 patients data were analyzed. Median age was 55 (33-72) years old with 53,1 % (n=26) patients being male. Two groups were similar, acoording to age, weight, office blood pressure, heart rate

(p>0,05), but there was higher numbers of diabetes melitus and coronary artery disease in group B. Mean prescribed antihypertensive drugs (A- 4,75; B- 6,52; p>0,05). In A group we observed significantly reduced BP (sABP 162,6mmHg to 149,6mmHg, p<0,01; dABP 100,8mmHg to 90,24mmHg, p=0,01) during 48 months. In B group: sABP 163,76 mmHg to 152,1mmHg, p=0,13; dABP 89,7 mmHg to 85,1 mmHg, p=0,54). In A group we observed significantly reduced carotid-femoral aortic pulse wave velocity (AoPWV) from 11.2 m/s to 10.0 m/s in 4 years (p=0,01). In second group AoPWV increased from 11,8 m/s to 12,8 m/s, but not significantly (p=0.34).

Conclusions: Patients with more comorbidities and receiving more pills are at higher cardiovascular risk and their blood pressure is more difficult to control, even after renal denervation procedure.

HYPERTENSIVE URGENCY, EMERGENCY AND KIDNEY FUNCTION

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Objective: The aim of this study was to determine risk factors for hypertensive crisis development just as an impact of the kidney function on it.

Design and method: From January to October 2019, 237 patients (109 males, 128 females) with hypertensive crisis were analyzed at the Emergency department in Clinical Hospital Merkur, Zagreb. We defined the hypertensive crisis as a rapid increase in blood pressure above 180/120mmHg (SBP range 182-260mmHg). Hypertensive crises were divided into two subgroups due to the evidence of end-organ damage. Elementary lab results and pulse wave velocity were checked in all patients.

Results: Hypertensive urgency was found in 184 patients (77.64%), emergency in 53 (22.36%). Comparison of these two subgroups showed that patients with an emergency were significantly older (70.51 vs. 64.44 years, p <0.01), had significantly elevated serum glucose levels (10.04 vs. 6.94mmol/L, p<0.0001), decreased glomerular filtration rate (CKD-EPI formula 75.96 vs. 59.15 mL/min/1.73m2, p<0.0001) and high heart rate (mean 96.32 vs. 77.17bpm, p<0.0001) which showed as the most significant risk factor. Body mass index didn't show any relevance in the hypertensive crisis development (31.26 vs. 30.58 kg/m2, p=0.18). Hypertensive emergency incidence increased with a decline in kidney function. Such events developed in 16.94% patients with CKD stage 1, 14.42% in stage 2, 34.61% in stage 3a, 50.00% in stage 3b, 60.00% in stage 4 and 50.00% in stage 5. Within main groups, patients were divided into two groups whether they used antihypertensive medication. A group of 53 patients was without medication (22.36%) of which 13 met criteria for a hypertensive emergency. Pulse wave velocity was much higher in patients with CKD-EPI < 45 ml/min/1.73m2 (13.01 vs. 10.74m/s, p=0.01). Even though female patients were significantly older (69.02 vs. 62.02years, p<0.0001), no other differences between genders were found.

Conclusions: Age, elevated plasma glucose and a decline in glomerular filtration rate combined with high heart rate values, but gender and body mass index independently are the main factors which are linked to the development of hypertensive emergency.

THE DEVELOPMENT OF RESISTANT HYPERTENSION INDEPENDENT OF THE PRECEDING PERIOD OF THE BLOOD PRESSURE CONTROL IS ASSOCIATED WITH THE INCREASED RISK OF CARDIOVASCULAR EVENTS AND DEATH

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Objective: Resistant hypertension (RH) is associated with the increased risk of cardiovascular events (CVEs); that excess risk is often attributed to the legacy of the previous period of uncontrolled blood pressures (BPs). We used the database of the ASCOT trial to evaluate the risk of CVEs (non-fatal myocardial infarction, fatal coronary heart disease, and fatal/non-fatal stroke) and death, after controlling for the cumulative mean of BPs for a preceding period of 2-years (using area-under-curve [AUC]).

Design and method: 18,926 hypertensive patients were initially followed up for the development of RH or not for a period of 2-years. During that period, we calculated the AUC of the cumulative mean BPs (AUCcmBPs) until the RH diagnosis or the end of the 2-year period if no-RH. These patients were then followed up from this new baseline for the risk of CVEs or death. We estimated incidence rates and developed a multivariable Cox regression model after adjusting for a-priori confounders (age, sex, socio-economic status, BMI, total cholesterol, HDL-cholesterol, systolic-BP at baseline, randomized treatment allocation, diabetes, other vascular diseases) and the AUCcmBPs. Interaction tests were done for those who were taking antihypertensive medications prior to the randomization or not.

Results: About one-third (n=5,660) developed RH by the end of 2-years. During the further median follow-up of 3.9 years, there were 1113 CVEs and 745 deaths. The incidence rate of CVE and death was higher in those with RH vs those without (34.8 and 18.9 per 1,000 person-years vs 24.0 and 15.4, respectively). In the multivariable model after controlling for the AUCcmBPs, those with RH, as compared to those without, had a significantly higher risk of CVE and death (HR: 1.15 [95% CI 1.03-1.27], p-value=0.010, and 1.16 [1.02-1.33], p-value =0.028, respectively). This excess in the risk didn't differ significantly between those who were on prior antihypertensive therapy or not (interaction test p-value=0.430 and p-value=0.310, respectively).

Conclusions: After accounting for prior BPs, the presence of RH is associated with the increased risk of CVEs and death; which could be because of the additional risk due to associated genotypical or phenotypical factors.

DIRECTLY OBSERVED ADMINISTRATION OF ANTI-HYPERTENSIVE MEDICATION PRIOR TO AMBULATORY BLOOD PRESSURE MONITORING – A USEFUL TOOL FOR INVESTIGATING 'RESISTANT HYPERTENSION'

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Objective: Non-adherence to anti-hypertensive medication is a well-recognized cause of apparent 'resistant hypertension'. We investigated whether directly observed administration (DOA) of anti-hypertensive medications, immediately prior to 24-hour ambulatory blood pressure monitoring (ABPM), would help exclude 'treatment resistance' potentially caused by medication non-adherence.

Design and method: Resistant hypertension was defined (as per UK guidelines) as a mean daytime blood pressure (BP) of 135/85 or more despite the use of three or more anti-hypertensives. All patients had 24-hour ABPM immediately after a morning clinic appointment. Patients attending our nurse-led hypertension clinic were requested in advance to not take their prescribed anti-hypertensives on the morning of their appointment, but to bring their medications with. Patients were then observed taking their medications prior to ABPM. Patients that did not follow these instructions or who had ABPM organised from a different clinic (without DOA) formed the control group. Proportions were compared with Chi-squares tests. Data analysis was performed using Microsoft EXCEL 2010.

Results: From November 2018 – October 2019, 53 patients had DOA before ABPM and were compared with 136 controls (see Table 1 for characteristics of each group). In the DOA group the average daytime BP was 138/83 with 38% having BP <135/85. In the control group average daytime BP was 141/86 with 27% having BP <135/85.
In total 54 patients were taking three or more anti-hypertensive medications. Table 2 compares the characteristics of these patients that underwent DOA (n=14) compared with those that did not (n=40). Of these patients, 50% that underwent DOA had a mean daytime BP of <135/85 compared with 20% in the control group (p=0.03).

	DOA (n=53)	Controls (n=136)
Mean age	51	46
% Male	53	46
% on ≥ 3 agents	26 (n=14)	29 (n=40)

Table 1: Baseline characteristics.
DOA: Directly observed administration.

	DOA (n=14)	Controls (n=40)
Mean age	57	58
% Male	43	55
% taking A,C and D*	57	53
Mean no. anti-hypertensives	3.9	3.7

Table 2: Patients on ≥ 3 anti-hypertensives.
DOA: Directly observed administration.
A: Angiotensin-converting enzyme inhibitor/angiotensin-2 receptor blocker; C: Calcium channel antagonist; D: Diuretic.
*These agents +/- additional medication.

Conclusions: Eliminating any effect of medication non-adherence by directly observed administration of prescribed anti-hypertensives immediately prior to ABPM leads to a lower rate of 'resistant hypertension' diagnoses. This strategy may therefore negate the need for further treatment and/or investigation in some patients.