P4781
Task sharing interventions for cardiovascular risk reduction and blood pressure changes in low-middle income countries. A systematic review and meta-analysis
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Background: One of the potential strategies to improve health care delivery in understaffed low-middle income countries (LMIC) is task sharing, where specific tasks are transferred from more qualified healthcare cadres to a lesser trained cadre. Hypertension is a major risk factors for cardiovascular disease but often it is unmanaged/appropriately.
Purpose: We conducted a systematic review and meta-analysis with the objective to identify, and evaluate the effect of task sharing interventions on blood pressure outcomes in LMIC.
Methods: Published studies (RCTs and observational studies) were identified via electronic databases such as PubMed, EMBASE, Cochrane Library, PsyCINFO, and CINAHL. We searched the databases from inception to June 2017, using search terms related to task shifting, and cardiovascular disease prevention in LMIC. All potential studies were grouped for meta-analysis.
Results: Although our search yielded 4566 records initially, only 19 studies met the eligible criteria. Two studies had more than two arms and they were treated separately. Most of the studies targeted lifestyle modification, and care coordination by involving nurses or allied health workers. In total, 21 comparison groups met the criteria in the meta-analysis. Task sharing interventions were effective in lowering systolic blood pressure (-5.45 mmHg; 95% CI: -7.74 to -3.16; c2=21,4, p<0.01, I2=89%) and diastolic blood pressure (-3.29 mmHg; 95% CI: -4.79 to -1.80; c2=8, p<0.01, I2=90%) with modest effect size in the random effect model. Although there was no publication bias found in the funnel plot, the test for publication bias was statistically significant (t = -1.39, df = 19, p-value = 0.18). The funnel plot test however showed asymmetry in the diastolic blood pressure model (t = -2.27, df = 17, p-value = 0.04). The overall quality of evidence based on GRADE was "low".
Task sharing interventions and SBP
Conclusion: Available data are not adequate to make recommendations on the role of task sharing strategies for the management of high blood pressure in LMIC. However, task sharing in LMIC could be the potential use of this strategy especially in terms of reduction in systolic and diastolic blood pressure levels. Our review calls for the need of well-designed, and large-scale studies to demonstrate the effect of task sharing strategy on blood pressure management in LMIC.
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P4782
The impact of microalbuminuria at risk of complications in patients with hypertension
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Aim: Determine the risk of developing thrombotic complications during one-year observation in patients with hypertension, depending on the presence of microalbuminuria, on the basis of a selection of a cohort of patients with hypertension.
Material and methods: 151 patients with arterial hypertension (grade 2) with concomitant ischemic heart disease and microalbuminuria (MAU) were examined. 1st group included 72 hypertensive patients (grade 2) with concomitant ischemic heart disease but without MAU. 2nd group included 79 hypertensive patients (grade 2) with concomitant ischemic heart disease without MAU. Venous blood samples were examined for: 1) coagulation activity: thrombin time (TT), activated partial thromboplastin time (aPTT), soluble fibrin-monomer complexes (SFMC), fibrinogen (Fg); 2)fibrinolytic activity: XII-a dependent fibrinolysis; 3)anticoagulant markers: partial thromboplastin time (aPTT), soluble fibrin-monomer complexes (SFMC), platelet aggregation; 4) indices of oxidative stress: antioxidant activity, lipid peroxidation levels. Our review calls for the need of well-designed, and large-scale studies to demonstrate the potential use of this strategy especially in terms of reduction in systolic and diastolic blood pressure levels.
Conclusions: Microalbuminuria, as an independent risk factor for cardiovascular complications, is associated with increased spontaneous aggregation of platelets more than 10%, increase in the content of SFMC higher than 4x10–2 g/l and a decrease in the AT-III content of less than 40%.

P4783
Arterial elastance predicts survival in low risk hypertensive patients
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Background: Risk stratification in low risk hypertensive patients is particularly difficult and unstudied despite of the vast number of those patients. Arterial elastance (EA) was defined as left ventricle end-systolic pressure (LVEDP) divided by stroke volume. Multivariable Cox proportional hazard was divided calculated adjusted to several risk factors and variables.
Results: Total time-risk was 7004 person-years. There were total of 165 composite endpoints over 10-year period and 56 deaths at the same time. In low-risk hypertensive patients, EA was only an echocardiography related parameter that predicted MACCE (HR=2.13; 95% CI: 1.04–4.37). In general population of hypertensive patients, left ventricle mass index had best predictive value, and was lost if calculated in low-risk patients (HR=4.45; 95% CI: 1.38–14.36 vs. HR=2.6; 95% CI: 0.68–9.91). EA best predicted value in low-risk patients especially without diabetes (HR=2.34; 95% CI: 1.07–5.13) or below 65y.o. (HR=2.8; 95% CI: 1.23–6.37). Influence on mortality was insignificant, probably because of low mortality rate in population.
Conclusions: In hypertensive patients with low comorbidities, thus low risk of mortality, EA emerges as valuable predictor, when regular risk factors fail to provide risk stratification. EA as surrogate of ventriculo-vascular coupling plays important role in HFpEF, and could provide risk stratification especially in patients with low risk. Further studies are needed.

P4784
A screening program for early vascular aging and hypertension in Austria
Background: Blood pressure (BP) control rates in Austria are largely unknown. The aim of our cross-sectional study was to screen for hypertension, using the novel concept of arterial stiffness and early vascular aging.
Methods and results: We acquired brachial waveforms with automated oscilometric devices in 45 public pharmacies and at 2 public health events in Upper Austria, a province with roughly 1 million inhabitants. Brachial BP was measured, and aortic pulse wave velocity (aPWV) was estimated, using age, systolic blood pressure, and waveform characteristics, with the validated ARCSolver algorithm. Using the 90th percentiles from a previous population study as age-specific cutoff value, we defined early vascular aging. In a subgroup, ambulatory blood pressure monitoring (ABPM) was performed to verify hypertension status.
Overall, 10 973 individuals participated (mean age 61.2 years, range 20–94, 67.6% were women. Mean BP was 133/83 mmHg, 38.1% of participants had elevated BPs (>140/90 mm Hg). A history of hypertension was reported in 37.3%, and 32.4% were on antihypertensives. Among 3960 participants with known hypertension, 55.1% had elevated aPWV, whereas among 6066 participants without known hypertension, 29.5% had elevated BPs. 19.9% of participants had a aPWV below 50th percentile, 42.8% between 50th and 90th percentile, and 37.3% were above the 90th percentile (early vascular
Hypertension mediated organ damage / Cardiotoxicity of drugs

P4785
Utility of the clock drawing test as cognitive screening in patients with arterial hypertension

Hypertension (HTN) is the most frequent cause of subclinical vascular injury of the brain. The impairment of executive function its characteristic clinical expression resulting from the disconnection between pre-frontal cortex and subcortical structures.

AIMS 1) To compare two cognitive tests, the mini-mental (MMSE) and clock-drawing test (CDT), as screening tools for cognitive impairment (CI) in hypertensive patients, 2) to know the prevalence of executive dysfunction in hypertensive patients and its association with different variables (treatment and control of the blood pressure, level of education and other cognitive proof).

Methods: A multicenter study (18 cardiology centers) that included hypertensive patients (both sexes, ≥18 years). Blood pressure was measured according to international standards. Patients were divided into 3 groups: treated/controlled PA <140–90 mm Hg (TC), treated/ non-controlled <140–90 mm Hg (TNC) and untreated (UT).

The educational level was recorded. MMSE and CDT tests were administered (cut-off CDT of 5 total point and MMSE according to age and education).

Results: 1414 hypertensive patients, average age 59.7±13.8 years (range 18–95 years), women (n=882, 62.3%). The mean blood pressure (BP) values of the sample were: systolic BP 143.6±12.2 mm Hg, diastolic BP 83.6±12.3 mm Hg. With 7 years of education: 44.5%, between 8 and 12 years: 33% and more than 12 years: 22.4%. The average MMSE score was 26.7±3.5 and the CDT 5.5±1.7. The prevalence of CI evaluated by the MMT (≥24: 20.7% (n=293) and by the CDT (≥5): 36.1% (n=511). Among hypertensive patients with normal MMT (≥24) 29.3% had abnormal TR. There was no association between the abnormal CDT and the treatment groups (TC, n=546, 36.2%; TNC / NT, n=869, 36.5%, p=0.56).

There was an inverse association between the level of education and the abnormal CDT (≤7 years education 45.8%, between 8 to 12 years 30.2% and >12 years 20.8%, p=0.000). The CDT correlated positively with the attention proof of the MMSE (Rho=0.40±0.03, p=0.000) and visuo-construction proof (pentagons; Rho=0.45±0.04, p=0.000).

Conclusion: CDT is a more useful tool MMSE in the cognitive screening of hypertensive patients. 1/3 of hypertensive patients with normal MMSE had abnormal CDT. The CDT was associated inversely with the educational level and positive with the attention and visual-construction proof of the MMSE.

P4786
Incremental prognostic value of cardiac-ankle vascular index as an arterial stiffness marker in patients with intermediate risk for cardiovascular disease
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Background: The cardiac-ankle vascular index (CAVI) is a non-invasive measurement evaluates arterial stiffness using the analysis of oscillometric waveform during cuff-inflation. Several studies reported that CAVI is associated with cardiovascular risk factors, while clinical relevance of CAVI as a surrogate marker of atherosclerosis has not been fully elucidated. Meanwhile, Framingham risk score (FRS) is widely used as the marker of cardiovascular risk.

Purpose: 1) to examine clinical implication of CAVI as a prognostic marker of cardiovascular events and (2) to evaluate whether CAVI has a potential to reclassify patients with intermediate risk assessed by FRS.

Methods: This prospective observational study included consecutive 422 patients with cardiovascular risk factors, but without known coronary artery disease (69±8 years, 63% men). CAVI was measured by the oscillometric method. Patients were divided into two groups according to CAVI as a cut-off value of 9.0, the incidence of cardiovascular events in the high CAVI group was significantly greater than that in the low CAVI group (p=0.001). After adjustment of confounding factors, CAVI over 9.0 remained associated with cardiovascular events (p=0.004), with a hazard ratio of 2.377 (95% CI: 1.301–4.315). Next, when patients with intermediate risk (n=217) were divided into two groups based on CAVI of 9.0, the Kaplan-Meier estimate showed that events occurred more frequently in higher CAVI group (9.3% and 29.1%, log-rank, P<0.009) and the C-statistic was 0.662. Multiple Cox analysis showed that, in the intermediate risk group, CAVI was an independent predictor of primary outcomes (HR 1.367 per 1 index, 95% CI 1.081–1.779, p<0.01).

Conclusion: The measurement of CAVI could be a useful predictor for cardiovascular events and for reclassification of patients with intermediate Framingham risk score.

P4787
Investigating the molecular mechanisms of carfilzomib-induced cardiotoxicity and the emerging role of metformin as a prophylactic therapy
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Background: Carfilzomib (Ctz) is an irreversible proteasome inhibitor, indicated for the treatment of relapsed/refractory multiple myeloma (R/R MM). In phase III trials, Ctz has been associated with significantly higher cardiotoxicity and heart failure rates compared to the standard treatment with the reversible inhibitor, bortezomib. Due to the severe adverse effects and the lacking data regarding the induced cardiotoxicity, there is an imperative need for the elucidation and abrogation of the underlying mechanisms of Ctz-induced cardiotoxicity.

Purpose: The purpose of this study was to investigate i) the molecular mechanisms of Ctz-induced cardiotoxicity and ii) to investigate the cardioprotective effect of metformin (Met).

Methods: Protocol 1: Male C57BL/6 mice, were randomized into: Control (N/S 0.9%, n=7) and Ctz group (n=8). Protocol 2: Male C57BL/6 mice were randomized into: Control (N/S 0.9%, n=8); Ctz (n=8) and Ctz+Met (n=10). Ctz (8 mg/kg ip) was administered every 48 hours and Met (140 mg/kg po) every 24 hours for 6 days. Fastening glucose levels were monitored. At baseline and at the end of treatments mice underwent echocardiographic assessment. Myocardial tissue samples were obtained for the analysis of proteasome peptides activity, protein phosphatase 2A (PP2A) activity and molecular signalling mechanisms.

Results: Administration of Ctz resulted in significant reduction of the chymotrypsin-like (CTL) proteasome activity in myocardial tissue and peripheral blood mononuclear cells of Ctz-treated mice vs controls (p<0.01). Protocol 1: Reduction in fractional shunting of Ctz could be observed in the Ctz group vs Control at Day 6 (39.87±0.47% vs 42.05±0.64% respectively, p<0.05). Ctz increased PP2A activity vs Control (p<0.05), without altering PP2A expression. A decrease in pAkt/tAkt (p<0.05), p4E-BP1/4E-BP1 (p<0.05), pAMPKα/AMPKα and an increase in the expression of NOS (p<0.01) was observed in the Ctz group vs Control. Protocol 2: Met did not reduce fasting glucose levels at 6 days in Ctz+Met compared to Control and Ctz groups. Echocardiographic assessment at day 6 revealed that Met reversed Ctz-induced reduction in the FS% in Ctz+Met vs Ctz group (43.45±0.54% vs 41.55±0.4% respectively, p<0.05). AMPKα phosphorylation was significantly increased in the same group compared to Ctz group (p<0.01).

Conclusion: The present study demonstrates that Ctz induces cardiac dysfunc-

P4788
5-Fluorouracil cardiotoxicity: the role of oxidative stress, apoptosis, inflammation and endothelial dysfunction
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Introduction: 5-Fluorouracil (5-FU) is a highly effective anticancer drug, widely...