PP088—NITROSONIFEDINE, A PHOTODEGRADATION PRODUCT OF NIFEDIPINE, SUPPRESS THE PROGRESSION OF DIABETIC NEPHROPATHY WITH THE ENDOTHELIAL DYSFUNCTION

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Introduction: Oxidative stress and endothelial damage are involved in the development and progression of diabetic nephropathy (DN). In this study, we investigated the effects of nitrosonifedine (NO-NIF) having antioxidative property on DN with the endothelial dysfunction.

Patients (or Materials) and Methods: KKAY mice were used as a model of developing type II diabetes mellitus with the endothelial dysfunction. NO-NIF (30 mg/kg/d) was administrated continuously by intraperitoneal injection for 4 weeks. Histologic changes in the kidney, urinary protein, urinary albumin, oxidative stress, and blood glucose levels were evaluated. Moreover, we also examined whether NO-NIF affected the kidney dysfunction in eNOS knockout mice.

Results: In NO-NIF–treated KKAY mice, the urinary protein and albumin were significantly decreased compared with nontreated KKAY mice. The pathologic analysis showed expanded glomerular mesangium in KKAY mice, which was suppressed by NO-NIF administration. However, NO-NIF had no effect on blood glucose in KKAY mice. NO-NIF decreased dihydroethidium staining in the kidney and 8-hydroxy-2-deoxyguanosine in the urine in KKAY mice. The expression of intercellular adhesion molecule-1, an endothelial cell damage marker, was decreased in the kidney by NO-NIF while the podocyte injury marker was not changed. The mRNA expression of TNF-α in kidney was also inhibited by NO-NIF. Furthermore, the administration of NO-NIF also suppressed the expansion of glomerular mesangial area and decreased urinary albumin in eNOS knockout mice.

Conclusion: NO-NIF prevents renal dysfunction associated with endothelial dysfunction independently of the blood glucose lowering, and it might be a potential drug for the prevention of DN.

Disclosure of Interest: None declared.

PP089—THE 3.5-YEAR MORTALITY IMPACT OF DRUGS IN SECONDARY PREVENTION OF MYOCARDIAL INFARCTION IN REAL-LIFE (INTERIM ANALYSIS OF THE EOLE COHORT)

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Introduction: Few studies have assessed the real-life impact of secondary prevention drugs on all-cause mortality postmyocardial infarction (MI), especially in countries with low incidence of MI. The objective of this interim analysis after 3.5-year of follow-up was to assess the real-life all-cause mortality impact of drugs reimbursed for MI secondary prevention in France: acetylsalicylic acid (ASA), antiplatelet agents (APA), beta-blockers (β-), angiotensin-converting enzyme inhibitors (ACEI), statins, and omega-3 supplementation (Om3).

Patients (or Materials) and Methods: Cohort study of patients with recent (≤ 3 months) acute MI included by hospital and nonhospital cardiologists, with 6-year follow-up. Vital status was obtained from the National death registry, and failing that by patient/relatives/physicians investigation. Drug exposure was defined using both physician and patient reports at inclusion. Cox proportional hazards model was used to estimate for each drug, mortality hazard ratio (HR) of exposed versus nonexposed patients, adjusted for gender, age, cardiovascular risk factors, other MI prevention drugs, and propensity score to be exposed at inclusion. Results presented concern an interim analysis after 3.5 years of follow-up.

Results: Between May 2006 and June 2009, 596 physicians included 5538 patients: mean age, 62.1 years; 77.6% male; 9.6% current smokers, 14.5% diabetic, 44.6% hypercholesterolemic, 43.6% hypertensive, and 8.2% with LVEF ≤ 50%. At inclusion, 97.5% were exposed to ASA, 91.0% to APA, 89.7% to β-, 71.1% to ACEI, 92.0% to statins, and 15.7% to Om3. The 3.5-year mortality was 7.8% (95% CI [7.1%–8.5%]) with an incidence rate of 23.2 per 1000 patient-years. Adjusted HR were: 0.98 [0.60–1.61] for ASA, 0.86 [0.60–1.24] for APA, 0.84 [0.63–1.11] for β-, 0.80 [0.61–1.03] for ACEI, 0.67 [0.45–1.00] for statins, and 0.82 [0.58–1.16] for Om3.

Conclusion: The 3.5-year interim all-cause real-life death reduction point estimates were close to those of large randomized controlled trials, except for ASA, for which almost all patients were exposed. The study’s statistical power will be sufficient to confirm or not these trends at the final 6-year analysis.

Disclosure of Interest: None declared.

PP091—COMPLEX REGULATION OF ALPHA-ADRENOCEPTOR-MEDIATED VASOCONSTRICION IN HUMAN INTERNAL THORACIC ARTERIES

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Introduction: Effective flow through conduit arteries is important both for in situ organ perfusion and for tissue function after surgical and other procedures for revascularization. Membrane-bound, calcium-independent phospholipase A2 (iPLA2) has been implicated in G-protein coupled receptor-mediated vasoconstriction in experimental studies using Sbromoenolactone (S-BEL) as a probe. However, the role of iPLA2β is unclear with regard to the regulation of vascular tone in humans. S-BEL selectively inhibits iPLA2β. It also inhibits other serine hydrolases, including phosphatidate phosphohydrolase-1 (PAP-1).

Patients (or Materials) and Methods: We studied human internal mammary (IMA) arteries obtained during coronary artery surgery and assessed iPLAβ in silico and responses in vitro to S-BEL, its enantiomer R-BEL, and propranolol of vessels preconstricted with phenylephrine (PE) to 80% of maximum response. All patients were undergoing surgery for treatment of ischemic heart disease and gave written informed consent to the study, which was approved by the local research ethics committee. Data are shown as means and standard errors. Data were compared by paired (Wilcoxon) or multi-way (Friedman) nonparametric tests.

Results: Compared with PE alone, contraction to PE increased during incubation of IMA segments in the presence of S-BEL 25μM (PE alone, 6.9 [2.4] [SE] mN; PE with S-BEL, 12.7 [2.5] mN; P = 0.028, Wilcoxon) in contrast to time-dependent decreased contraction to