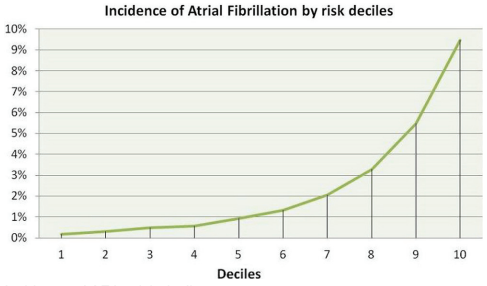
data warehouse. The study population consists all adult members older than 40 years, with no previous diagnosis of AF.
Within the five years following the index date, we have compared the baseline characteristics of patients who developed AF with those who did not. We calculated the 5 years risk to develop AF for every individual in our cohort, creating a risk score to identify those at high risk.
Results: The research population included 1,256,617 patients, with an AF incidence rate of 2.4%.
The best predictors to develop AF within 5 years were: Age, Gender, Congestive Heart Failure, Hypertension, anti-hypertensive treatment, BMI and Ischemic Heart Disease. The Logistic Regression Model we created utilizing those risk factors showed a 9.5% incidence of AF within the highest decile and a 14.3% within the highest percentile, a lift of 3.9 and 5.9 respectively, compared to the risk in the overall population.



Incidence of AF by risk deciles

Conclusion: Our risk score model for detecting AF consists of classic and simple risk factors. We suggest that systematic screening for AF in asymptomatic patients, in accord with our risk score model, has the potential of helping to identify patients likely to benefit from more intense screening.

P1087 | BEDSIDE
Adding risk factors profile to pain characteristics does not increase the predictive power for coronary artery disease in chest pain patients

S. Thiru, A. Alexopulos, A. Chenzbraun. *The Royal Liverpool University Hospital, Liverpool, United Kingdom*

Background: The likelihood of coronary artery disease (CAD) is estimated by historical prediction models using symptoms, demographics and risk factors profile (Duke Clinical Score) or demographics and symptoms only (Diamond Forrester model). Data are accumulating suggesting that these prediction models grossly overestimate CAD prevalence in today patients. This is a prospective study to assess the actual CAD prevalence in patients referred to a chest pain clinic and the comparative performance of the two models and of using pain characteristics only in predicting CAD in these patients.
Methods: 1376 consecutive patients (age: 58±12 years) were reviewed in a dedicated chest pain clinic. Patients were assigned to five estimated CAD likelihood groups: <10%, 10–29%, 30–60%, 61–90% and >90% using the Duke Clinical Score and to three CAD likelihood groups: <15%, 15–85% and >85% using the Diamond-Forrester model. Patients were diagnosed as having CAD when either obstructive (>70%) coronary stenoses were demonstrated by invasive angiogram or CTCA or a functional test was positive. The observed CAD prevalence was compared with the predicted one and comparative diagnostic performance was assessed with ROCs.
Results: 652 pts. (47%) had non-anginal CP, 412 pts. (30%) had atypical AP and 312 (23%) had typical AP. 417 pts (30%) were not investigated for CAD due to non-anginal symptoms and/or low CAD probability. Investigations were completed in 858/959 pts. The actual CAD prevalence was 21% vs. a Duke Clinical Score predicted one of 53% and an Diamond-Forrester model predicted one of 36% (p<0.001). Both models had modest predictive abilities with AUCs of 0•695 and 0•693, respectively (p=ns) and did not show useful clinical superiority over a prediction model using pain characteristics only (AUC: 0•65) – Figure 1

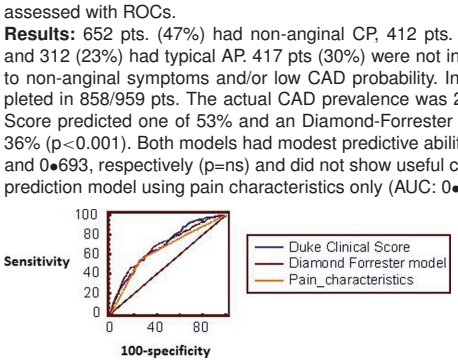


Figure 1

Conclusions: 1. In this prospective study of patients investigated for chest pain, the actual prevalence of significant CAD was much lower than the one predicted by historical predictive diagnostic models.
2. The use of risk factors and demographic profile in addition to pain characteristics was not found to improve diagnostic accuracy.
3. Until an accurate predictive model is validated, the results of this study suggest that a "binary" assessment whereby an investigation pathway is triggered for all patients in whom ischemic chest pain cannot be reasonably excluded using pain characteristics might be a better approach than assigning the patients to CAD likelihood groups and tailoring the investigation strategy as per the estimated pre-test probability.

P1088 | BEDSIDE
Glycemic variability, but not Hb1Ac, is associated with high SYNTAX scores at the acute phase of myocardial infarction in diabetic patients treated with insulin infusion

M. Benalia[1], C. Guenancia[1], G. Porot[1], M. Zeller[2], F. Bichat[1], J.M. Petit[3], B. Verges[3], Y. Cottin[1]. *[1]University Hospital Center, Department of Cardiology, Dijon, France; [2]University of Burgundy, Laboratory PEC2, Dijon, France; [3]University Hospital Center, Department of Endocrinology and Diabetology, Dijon, France*

Background: In acute myocardial infarction (AMI), higher levels of blood glucose at admission are associated with lower survival rates but randomized studies that have examined the impact on mortality of lowering blood glucose with intravenous insulin infusions (IVII) have presented conflicting results. Glucose variability (GV) is also an independent prognostic factor and physiological studies have suggested several mechanisms by which GV adversely impacts prognosis in the setting of AMI, including 1/ rapid progression of non-culprit lesions, 2/ coronary plaque vulnerability, 3/ left ventricular remodeling. The objectives of this study were to identify factors associated with sustained high GV among diabetic patients admitted for AMI treated with IVII and to evaluate the association of GV with AMI characteristics.
Methods: All consecutive diabetic patients admitted to our University Hospital for AMI between January 2014 and March 2016 and who received IVII were included. The mean amplitude of glycemic excursions (MAGE) was calculated within 2 days after the AMI in order to evaluate GV. The population was divided into tertiles according to MAGE, and bivariate and multivariate analyses were performed.
Results: Among the 1305 AMI admitted during the analysis period, 196 patients matched the inclusion criteria. The mean age of the population was 71.3±12.1 years, and 31% were women. The mean MAGE was 0.72±0.41. When compared with the other two MAGE tertiles, patients with the the highest MAGE (last tertile) were more often women, and more often had diabetes previously treated with insulin and history of renal failure. Moreover, both glycemia at admission and Hb1Ac levels were significantly higher in these patients. Regarding AMI parameters, the patients in the highest MAGE tertile had higher SYNTAX and GRACE scores, and lower systolic and diastolic blood pressure. After multivariate analysis, four parameters were significantly and independently associated with the highest tertile of MAGE: female sex (OR (95% CI): 5.67 (2.29–14.02) p<0.001), Hb1Ac (OR (95% CI): 1.77 (1.33–2.34) p<0.001), Systolic blood pressure (OR (95% CI): 0.99 (0.97–1), p=0.049) and SYNTAX score (OR (95% CI): 1.05 (1.01–1.08), p=0.007).
Moreover, after multivariate analysis, age (OR (95% CI): 1.05 (1.02–1.09) p=0.001), history of stroke (OR (95% CI): 6.25 (1.65–23.5) p=0.007) and the highest tertile of MAGE (OR (95% CI): 2.60 (1.24–5.41) p=0.011) were independently associated with the highest tertile of the SYNTAX score, whereas Hb1Ac was not.
Conclusion: Our study shows that GV was mainly associated with diabetes-related factors. In addition, GV, but not HbA1c, was independently associated with a high SYNTAX score. Our findings suggest that assessment of blood GV could contribute to the identification of high-risk diabetics and become a therapeutic target in primary and secondary prevention.

P1089 | BEDSIDE
Improving the value of clinical variables in the assessment of cardiovascular risk using Artificial Neural Networks

L.E. Juarez-Orozco[1], R.J.J. Knol[2], C.A. Sanchez-Catasus[3], F.M. Van Der Zant[2], J. Knuuti[1]. *[1]Turku University Hospital, PET Center, Turku, Finland; [2]Cardiac Imaging Division Alkmaar, Northwest Clinics, Department of Nuclear Medicine, Alkmaar, Netherlands; [3]University Medical Center Groningen, Nuclear Medicine and Molecular Imaging, Groningen, Netherlands*

Background: There is a substantial number of interrelated variables that have been associated to coronary artery disease (CAD) and to an increased risk of adverse cardiovascular outcomes. Currently, machine learning algorithms such as Artificial Neural Networks (ANN) constitute flexible models capable of characterizing complex relationships between numerous variables. ANN can be trained and applied to complex classification problems. On the other hand, PET perfusion imaging studies have demonstrated that a hampered myocardial perfusion reserve (MPR) (<2.0) conveys a significant risk for adverse cardiovascular outcomes. The present study generated and applied an ANN for the prediction of a PET-measured hampered MPR based on simple available predictors in patients with intermediate risk of CAD.
Methods: We included 1,241 patients with no previous MI or revascularization referred to 13N-ammonia PET for suspected ischemia. They were randomly divided into training, testing and holdout datasets (6:2:2). Demographic (sex, age, BMI and family history of CAD), clinical (chest complaints, diabetes, smoking, dyslipidemia, hypertension, rest heart rate [HR] and resting blood pressure [BP]) and complementary diagnostic data (Duke score, abnormal rest ECG, abnormal stress ECG, stress HR, % of max HR, stress BP, rest LVEF and stress LVEF) was retrieved. A multilayer perceptron analysis constructed the feed forward back propagation ANN with a hyperbolic tangent as the activating function. The net-

work was trained and tested to classify the probability of cases of presenting a reduced MPR (<2.0). The ANN was then applied to the holdout dataset. The area under the curve (AUC) and normalised importance (NI) of the predictors were reported. Additionally, ensemble boosting of the ANN was performed to explore for accuracy improvement.
Results: The resulting ANN architecture used one hidden layer (with 6 nodes) and it showed a stable overall accuracy of 75% in the divided datasets, showing adequate generalisation. The ANN's AUC was 0.77 and the 5 most relevant predictors for network's construction were rest HR, age, stress, LVEF, BMI and stress HR (with a NI=100%, 63%, 41%, 32.5% and 31.3%). The ANN was generally more accurate when classifying a patient with a normal MPR than one with an abnormal MPR. Ensemble boosting, which iteratively created and improved the network classifiers achieved an increment of the overall accuracy to 84% when classifying new patients.
Conclusion: This study suggests that machine learning in the form of an ANN may be utilised to improve identification patients who will demonstrate a reduced MPR, based on simple and readily available clinical data, with a good overall accuracy (84%). This opens the possibility to improve the characterisation of patients at risk based on numerous and interrelated clinical variables. Further research into the application of ANNs with emerging and relevant predictors of cardiovascular risk is warranted.

P1090 | BEDSIDE
The association of cardiac valvular calcification, protein-energy wasting and inflammation status with cardiovascular- and all-cause mortality in incident haemodialysis patients

H. Takahashi[1], H. Ishii[2], T. Aoyama[3], D. Kamoi[3], N. Umemoto[3], T. Sakakibara[3], Y. Kumada[4], T. Murohara[2]. *[1]Fujita Health University School of Medical Science, Toyoake, Japan; [2]Nagoya University Graduate School of Medicine, Cardiology, Nagoya, Japan; [3]Nagoya Kyoritsu Hospital, Cardiology, Nagoya, Japan; [4]Matsunami General Hospital, Cardiovascular Surgery, Kasamatsu, Japan*

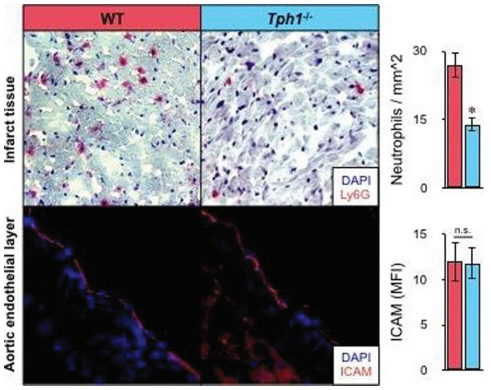
Background: Cardiac valvular calcification, frequently seen in end-stage renal disease (ESRD) patients, potentially reflects systemic atherosclerosis. Protein-energy wasting (PEW) or malnutrition is also prevalent, and associated with increasing cardiovascular (CV) risk in this population. Currently, the PEW was considered to be due to inflammatory process rather than poor nutritional intake. We investigated the association of valvular calcification, PEW and inflammation, and their joint role with prediction of CV- and all-cause mortality in ESRD patients at starting haemodialysis (HD) therapy.
Methods: A total of 1,351 ESRD patients who electively started HD therapy were screened by echocardiography. Valvular calcification was defined as bright echoes >1mm on one or more cusps of the aortic and/or mitral valve. Geriatric nutritional risk index (GNRI) which calculated from serum albumin levels, body weight and height as a surrogate marker of the PEW, and C-reactive protein (CRP) were measured at the same point. Patients were followed-up for 10 years.
Results: Declined GNRI and elevated CRP levels were independently associated with presence of valvular calcification [odds ratio (OR) 0.97, 95% confidence interval (CI) 0.96–0.99, p=0.0002 and OR 1.09, 95% CI 1.01–1.18, p=0.0033, respectively]. During follow-up period (median of 63 months), 322 patients (23.8%) died including 141 (10.1%) CV cause. Cox multivariate analysis revealed that valvular calcification [hazard ratio (HR) 1.31, 95% CI 1.04–1.67, p=0.021], GNRI<92.0 as a median value (HR 1.65, 95% CI 1.31–2.09, p<0.0001) and CRP>1.9 mg/l as a median value (HR 1.73, 95% CI 1.37–2.19, p<0.0001) were independent predictors for all-cause mortality. When patients were divided into groups according to number of these three risk factors, 10-year Kaplan-Meier survival rate was 85.9%, 75.1%, 55.7% and 32.7% among groups with no risk factor, any 1 risk factor, any 2 risk factors and all risk factors, respectively (p<0.0001 for trend). After adjustment for other confounders, patients with any 1, any 2 and all risk factors had 1.58-fold (95% CI 0.97–2.72), 2.41-fold (95% CI 1.50–4.12) and 3.86-fold (95% CI 2.38–6.63) higher risk for mortality compared to those without any risk factor, respectively (p<0.0001 for trend). Similarly, the freedom rate from CV mortality was 92.4%, 88.1%, 76.1% and 59.7% (p<0.0001 for trend), and patients with all risk factors had 3.68-fold (95% CI 1.86–8.12, p<0.0001) higher risk for CV mortality compared to those without any risk factor.
Conclusions: Presence of cardiac valvular calcification was closely associated with both declined GNRI and elevated CRP levels in ESRD patients just starting HD therapy. Combination of these predictors was also additively associated with increasing risk of both CV- and all-cause mortality. These results clearly manifested the so-called malnutrition, inflammation and atherosclerosis (MIA) syndrome in this high-risk population.

ISCHAEMIA AND PROTECTION

P1091 | BENCH
Platelet serotonin aggravates myocardial reperfusion injury via degranulation

M.M. Mauler[1], N.H. Herr[2], C.S. Schoenichen[2], T.W. Witsch[2], T.M. Marchini[2], C.H. Haerdtner[2], C.K. Koentges[2], D.S. Stallmann[2], H.B. Bugger[2], D.W. Wolf[2], I.A. Ahrens[2], K.L. Ley[3], C.B. Bode[2], I.H. Hilgendorf[2], D.D. Duerschmied[2]. *[1]University of Freiburg, Faculty of Biology, Heart Center, Freiburg, Germany; [2]University of Freiburg, Heart Center, Freiburg, Germany; [3]La Jolla Institute for Allergy and Immunology, La Jolla, United States of America*

Background: Inflammation in the vascular compartment during reperfusion after acute myocardial infarction comes with a burst of neutrophils migrating into the heart. Serotonin (5-hydroxytryptamine; 5-HT; synthesized by tryptophan hydroxylase 1, TPH1) mediates neutrophil recruitment. Depletion of platelet serotonin attenuates this effect and leads to a protective phenotype upon inflammation.
Purpose: Evaluation of serotonin mediated effects on acute phase inflammation during myocardial reperfusion injury.
Methods: MI was induced in vivo for 30 minutes in C57Bl/6 (WT) and Tph1 deficient mice, followed by 24 hours of reperfusion. Heart function and infarct size was evaluated. Heart tissue was analyzed for cytokine expression and migrated inflammatory cells. Blood was taken to assess platelet neutrophil complexes as well as integrin and selectin expression on circulating neutrophils and platelets using flow cytometry.
Ex vivo heart function was analyzed using the isolated working heart assay.
Results: Plasma serotonin peaked 24 hours after in WT mice (150±10 ng/mL) and reached normal levels after 2 days (90±2 ng/mL). Heart function in Tph1–/– mice compared to WT after surgery was improved accompanied by a significant reduction of infarct size (35±3 in Tph1–/–; 53±5 in WT; % area at risk). This effect was absent in the ex vivo working heart mode. WT mice revealed increased MPO and TNFα expression within the heart and neutrophil content in the AAR was reduced in Tph1–/– mice (14±2 vs. 28±3 in WT per mm^2 tissue) whereas monocytes were similar. Aortic root ICAM expression was similar in both groups (12±2 vs. 13±3% MFI) (Fig.1). Depletion of neutrophils by injection of an anti Ly6G antibody protected WT mice and reduced infarct size to 37±4%AAR.
Looking at surface marker on neutrophils, we found a decreased expression of CD11b in Tph1–/– mice (30±5%) compared to WT mice (expression set 100%).
In vitro analysis of neutrophils revealed that stimulation with 5-HT leads to increased surface CD11b and induces degranulation of neutrophils as indicated by electron microscopy.
We could reproduce our in vitro findings in human neutrophils and also found a correlation of plasma 5-HT and neutrophil CD11b in ACS patients (r=0,846).



Conclusion: Depletion of platelet serotonin greatly improves the outcome after I/R injury and leads to decreased infarct size and better heart function. This is contributed to an anti-inflammatory phenotype that comes with decreased neutrophil migration. We could identify neutrophils as a major contributor to myocardial reperfusion injury. Serotonin induces degranulation of neutrophils which results in increased CD11b expression on the cell surface. CD11b is one of the major mediators neutrophil adhesion to endothelial cells, which explains the pro-inflammatory properties caused by serotonin. Targeting serotonin-neutrophil interactions might open new strategies to control the inflammatory aspect of reperfusion injury.

P1092 | BENCH
ROS-dependent store-operated Ca entry does not increase diastolic Ca in isolated ventricular myocytes

M. Goetz, C. Schach, L.S. Maier, D. Endemann, S. Wagner. *University Hospital Regensburg, Department of Internal Medicine II, Regensburg, Germany*

Rationale: Reactive oxygen species (ROS) are known to disturb intracellular Ca handling, which contributes to ischemia-reperfusion injury (IRI). ROS have been shown to stimulate store-operated Ca entry (SOCE) but the relevance in cardiomyocytes is unknown.