vs 37%); 20% of Asian patients received no antithrombotic treatment vs 12% of those in Europe ($p<0.001$ for overall treatment). VKA use was lower in Asia than in Europe irrespective of risk level (CHA2DS2-VASc <2: 35% vs 58%, respectively, $p<0.001$; score ≥2: 42% vs 67%, $p<0.001$). Despite lower overall use of VKAs in Asia, stroke/systemic embolism rates were similar; risk of major bleeding was lower (Table).

Conclusion: These multinational observational data from the GARFIELD Registry suggest that a more risk-based approach to VKA treatment at diagnosis may be applied in Asia versus Europe, resulting in a lower rate of bleeding and equivalent rate of stroke/systemic embolism.

P4278 | BEDSIDE
Guidance adherent dabigatran etexilate treatment versus warfarin in the RE-LY population: an analysis on the basis of the European label recommendations for dabigatran etexilate

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Purpose: In the RE-LY trial, patients were randomized to treatment arms independent of baseline characteristics; dabigatran 150 mg twice daily (BID; D150) was associated with significantly fewer strokes and dabigatran 110 mg BID (D110) with significantly fewer major bleeding events, compared to well controlled warfarin. The European (EU) label recommends D150 in patients <80 years without an increased risk for bleeding or concomitant verapamil and D110 in other patients. In this analysis of the RE-LY dataset, we simulated how dabigatran, when used according to the EU label, would compare to well controlled warfarin.

Methods: In this post hoc, non-randomized analysis, we simulated the outcomes of patients receiving dabigatran with a dose selected according to the EU label and compared them to the warfarin-treated patients.

Results: "EU label simulated dabigatran treatment" was associated with significant reductions in stroke and systemic embolism, haemorrhagic stroke, death and vascular death compared to warfarin; also with significant reductions in major and life-threatening bleeding and intracranial haemorrhage, but not gastrointestinal major bleeding, compared to warfarin (table). EU label simulated dabigatran outcomes were not significantly different from those of patients receiving D150 in RE-LY.

Endpoint	Annual rate per 100 person years		
	EU label simulated dabigatran treated	Warfarin treated (as randomized)	Hazard ratio (95% CI)
N (intention to treat)	6,004	6,022	–
Primary: stroke/systemic embolism	1.27	1.71	0.74 (0.60, 0.91)
Haemorrhagic stroke	0.08	0.38	0.22 (0.11, 0.44)
Death	3.55	4.13	0.86 (0.75, 0.98)
Vascular death	2.16	2.69	0.80 (0.68, 0.95)
N (safety)	5,981	5,998	–
Major bleeding events	3.02	3.55	0.85 (0.73, 0.98)
Life-threatening major bleeding events	1.28	1.75	0.72 (0.58, 0.91)
Intracranial haemorrhage	0.22	0.77	0.28 (0.17, 0.45)
Any bleeds	17.53	19.75	0.86 (0.81, 0.92)

Conclusion: This post hoc, non-randomized analysis of the RE-LY trial suggests that "EU label adherent dabigatran treatment" may be associated with superior efficacy and safety compared to warfarin.

P4279 | BEDSIDE
Renal adiponectin as a biomarker of kidney disease in stable anticoagulated atrial fibrillation patients

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Background: A close relationship between atrial fibrillation (AF) and kidney disease (KD) has been observed. This relation is probably related to share physiopathological mechanisms as inflammation and atherosclerosis. KD is associated with a high prevalence and incidence of AF, thus increasing the risk of stroke and thromboembolic events. There are limited biomarker data that predict the impairment of renal function in patients with AF. The aim of the study was to study the relationship of two biomarkers associated with atherosclerosis and inflammation (i.e. adiponectin and interleukin-6, IL-6) with the impairment of renal function in a cohort of patients with stable AF.

Methods: 835 patients with AF on stable oral anticoagulation from our out-patient anticoagulation clinic (all INR 2.0-3.0 during previous 6 months) were enrolled (50% male, median age 75 years [70-81]). Estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease equation (MDRD) at baseline and 2 years later (renal function follow-up in 656 patients). Adiponectin levels were measured by commercial ELISA and IL-6 levels by automated determinations (ROCHE diagnostic). The optimal cut-off were established using ROC curves (IL-6 >4.42 pg/mL and adiponectin <3066 ng/mL).

Results: At baseline, median eGFR was 70.25 ml/min/1.73 m^2 (54.41-83.69). At baseline, 29 patients had severe KD (eGFR<30ml/min/1.73m^2) and were excluded for future analysis. 182 patients (28%) had a decrease in eGFR >10 ml/min/1.73m^2 during the follow-up and 14 (2%) deteriorated to <30 ml/min/1.73m^2. On univariate analysis, heart failure, baseline eGFR, ischemic heart disease, adiponectin and IL-6 were associated with the development of severe KD. On multivariate analysis, baseline eGFR [OR: 3.03 (1.07-8.56); p=0.036], heart failure [OR: 4.29 (1.12-16.46); p=0.034], and adiponectin <3066 ng/mL [OR: 4.53 (1.43-14.37); p=0.010] were significant predictors, but not IL-6 [OR: 3.11 (0.90-10.81); p=0.074].

Conclusions: Deterioration of renal function in patients with AF is not a rare process; but severe impairment is infrequent. Adiponectin predicts the development of severe KD, which might be considered to be another adverse atherosclerotic event in patients with AF.

CARDIOVASCULAR DISEASE, DIABETES AND METABOLIC SYNDROME

P4281 | BEDSIDE
Effective prevention of adverse cardiac events in patients, undergoing vascular operations

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Purpose: To study role of atorvastatin in prevention of cardiac complications in patients with atherosclerosis, undergoing vascular surgery by correction of nitrosative stress, platelet aggregation and inflammation.

Methods: 130 patients with atherosclerosis, undergoing Aortafemoral Bypass (AFB) operation or abdominal aortic aneurysm repair were included in the study. Patients were divided into two groups. 1 group – (n=64) recived standart therapy, 2 group (n=66) – patients took in addition atorvastatin 60 mg per day during 14 days before operation. The nitrosative stress was determined by the level of 3-nitrotyrosine (3-NT). Platelet function was estimated by ADP-induced platelet aggregation and the plasma level of soluble CD-40 ligand (sCD40L). Biomarkers for inflammation included hsCRP, secretory phospholipase A2 type IIA (sPLA-A2 IIA). Blood samples were collected before and after treatment, after operation on 1st, 15th day. Control group (CG) – 30 healthy people.The intra- and postoperative cardiac complications were determined by clinical signs, electrocardiography monitoring, measuring troponin I.

Results: We found a significant increase in baseline levels of 3-NT, markers for aggregation and inflammation in both groups of patients in comparison with CG. After treatment in the 2nd group there was decrease in level of 3-NT (22%, $p<0.001$), ADP-induced platelet aggregation (10%, $p<0.01$), sCD40L (36.4%, $p<0.001$), hs-CRP (34%, $p<0.001$), sPLA- A2 IIA - (15.7%, $p<0.01$). In the 1st group significant changes were not observed. On the first and fifteenth day after operation indicators of inflammation, nitrosative stress and platelet aggregation were significantly less in the 2nd group than in the first. We found decrease in the rate of perioperative cardiac complications in the 2nd group in comparison with the 1st one (difference was 15.82%, p=0.025). We did not observe fatal myocardial infarction and acute heart failure in the second group.

Conclusions: Preoperative atorvastatin at high dose reduced cardiac complications after AFB operation and abdominal aortic aneurysm repair. It is connected with significant decrease in the level of nitrosative stress, platelet aggregation and inflammation.

P4282 | SPOTLIGHT 2013
Cyc-C is superior to creatinine in the early diagnosis of contrast-induced nephropathy

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Background: Contrast-Induced Nephropathy (CIN) is associated with prolonged hospitalization and serial measurements of creatinine should be monitored in all patients at risk. Because of the delayed increase in creatinine, CIN may be overlooked. The aim of this study is to assess whether changes in Cystatin C (CyC) after 48 hours from contrast media exposure is a reliable indicator of acute kidney injury and the validity of a risk scoring tool for CyC based CIN.

Methods: We enrolled 121 patients for whom coronary angiography were planned. The risk score for CIN was calculated and serum creatinine and CyC were measured before and 48 hours after coronary angiography. CyC and creatinine based CIN was calculated as a 25% increase from baseline within 48 hours from contrast media exposue.

Results: Mean serum CyC and creatinine concentrations were found to be 0.88±0.27 mg/dL and 0.79±0.22 mg/dL, respectively before the procedure and 1.07±0.47 mg/dL and 0.89±0.36 mg/dL, respectively 48 hours after contrast me-

Table 1. Mean Risk Scores in CyC based and sCr based CIN groups

			Mean±SD	p
Mehran Risk Score	sCr	≤25%	2.51±3.03	p=0.425
		>25%	3.60±4.12	
	CyC	≤25%	1.93±2.88	p<0.001
		>25%	4.00±3.47	

dia exposure (p<0.001). CyC based CIN occured in 44 patients (36.36%) and sCr based CIN occured in 20 patients (16.52%) after the procedure. Mean risk score was found to be 4.00±3.478 and 3.60±4.122 for CyC based CIN and sCr based CIN, respectively and found to be significantly increased in CyC based CIN group (p<0.001) (Table 1).
Conclusions: CyC measurement 48 hours after contrast media exposure is superior to serum creatinine measurement for the diagnosis of CIN and Mehran risk scoring tool is in good correlation with CyC increase for the prediction of CIN.

P4283 | BEDSIDE
Improving quality of care and financial burden in cardiology: a new approach with checklist based clinical pathways - first results

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Purpose: Clinical pathways (CP) have increasingly been introduced into surgery for standardized elective procedures. The aim of CPs is to enhance effectiveness and quality of care by guideline specific and standardized treatment and to subsequently reduce health care costs. Due to higher disease complexity and less standardized treatment approaches, cardiology and other specialties of internal medicine have so far only seen sporadic introduction of CPs.
Methods: In order to study feasibility of CP implementation into the clinical routine of a German university cardiology department, a novel checklist based CP system was broadly introduced. Key elements were 14 disease-specific CPs each detailing relevant diagnostic and therapeutic procedures and mandatory safety checks. Overall goal was to enhance standardization and cross-functional workflow transparency and thereby quality of patient care. Aim of this study was to prove CP-implementation feasibility and to evaluate clinical burden measured in average length of hospital stay (ALOS). Results were measured after 12 months of CP use (> 4500 patients included) and compared to pre CP introduction.
Results: Evaluation of used CP documents showed high compliance levels for CP use among staff (CPs used in > 95% of patients) while surveys for all involved functions underlined usability. Following CP introduction no significant change in ALOS was found in "high-volume diseases" (n=380 to 780 per year) e.g., angina pectoris (LOS +2,0%; p=0,78), myocardial infarction (-3,0%; p=0,63) or heart failure (-0,1%; p=0,17), while there was significant LOS-reduction for Afib (-4,9%; p = 0,01). Hypertensive urgency patients showed an increase in LOS (+16,9%; p<0,001) while "low-volume diseases" (n=29 to 150) revealed substantial LOS reductions (syncope: -23,1%, p<0,001; DVT: -20,8%, p=0,33; PE: -10,2%, p=0,07).
Conclusions: We showed feasibility of successful CP introduction within internal medicine by developing a novel checklist based approach built on cross-functional treatment guidance, transparency and regular risk checking. Significant ALOS-reduction for less frequent diseases were shown, further standardization of high-volume diseases seems less promising. LOS increase after CP introduction in hypertensive urgency can most likely be attributed to increased diagnostic screening for secondary hypertension. Since long hospital stays are an increasingly relevant burden for patients, care providers and payers, a broad implementation of the introduced CP approach could be an important lever in lasting quality of care improvements within cardiology.

P4284 | BEDSIDE
Pre-diabetes is a disease associated with significant cerebro and cardiovascular structural and functional abnormalities

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Purpose: To examine whether pre-diabetes is a risk factor for cerebro and cardiovascular structural and functional abnormalities (abn.), i.e. abn. small artery stiffness (C2) and abn. Carotid Intima Media Thickness (CIMT).
Methods: We screened 2236 asymptomatic subjects, age 23-80, for CVD risk using Early CVD Risk Score (ECVDRS). ECVDRS consists of 10 tests: C1 and C2, BP at rest and post mild exercise (PME), CIMT, abdominal aorta and left ventricle ultrasound, retinal photography, microalbuminuria, ECG, and pro-BNP. Euglycemia (EG), pre-diabetes (PD), and diabetes (DM) were defined according to the ADA criteria. Comorbidities (CM) were defined as elevated cholestrol, BP, waist circumference.
Results: Among the subjects screened, 73% (1642 of 2236) had EG, 27% (444 of 1642) of which had no CM; 22% (485 of 2236) had PD, 13% (63 of 485) of which had no CM; and 3% (74 of 2236) were diabetic, 3% (2 of 74) of which had no CM. 93% (450 of 485) of subjects with PD and 28% of the subjects with DM (21 of 74) were not taking antidiabetic medications. The presence of CVD abnormalities among the groups with EG and PD without CM is shown on table 1.

	EG w/o CM 27% (444 of 1642)			PD w/o CM 13% (63 of 485)		
	Male 39% (175 of 444)	Female 61% (269 of 444)	Total	Male 60% (38 of 63)	Female 40% (25 of 63)	Total
Abn. CIMT	13% (22 of 175)	20% (55 of 269)	17% (77 of 444)	21% (8 of 38)	24% (6 of 25)	22% (14 of 63)
Abn. C_2	35% (62 of 175)	24% (65 of 269)	29% (127 of 444)	53% (20 of 38)	40% (7 of 25)	43% (27 of 63)

Table 1

Conclusions: 1. PD is a disease associated with substantially greater structural and functional abnormalities than EG, particularly abn.C2. The relationship between increased glucose levels and abn. C2 holds even when controlling for CM.
2. The difference in the prevalence of abn. C2 between EG and PD subjects is statistically significant (p = 0.0350).
3. PD is prevalent in the asymptomatic subjects (22%) screened.
4. The presence of abn. CIMT in PD subjects, as compared to EG subjects, is greater in males than females (4% difference). Whether this is due to the protective, hormonal effects in female or other factors may be subject for future studies.

P4285 | BEDSIDE
Genetic polymorphisms associated with the development of type 2 diabetes mellitus

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Type 2 diabetes mellitus (T2DM) constitutes a worldwide health problem associated with strong cardiovascular risk. There are environmental factors that contribute for the development of this disease, such as obesity or sedentary life. However, individuals with normal weight can have T2DM and, on the other hand, many of the obese individuals will not develop diabetes, suggesting that it is compelling. the evaluation of other variables, such as genetic factors.
Objective: Our study aims to investigate genetic polymorphisms associated with the T2DM onset in a Portuguese population.
Methods: We performed a case-control study with 1938 Caucasians which 548 were diabetic type 2 patients (classified as diabetic according to the European Association for the Study of Diabetes) and 1390 were controls, with no significant difference in age. Blood samples for genetic analysis were collected, from both groups, in order to evaluate 18 genetic variants previously described as being associated to hypertension, obesity, diabetes or coronary disease as PON1 Q192R and PON1 L55M, KIF6 T/A, HNF4A C/G, FTO A/C, TAS2R50 A/G, PCSK9 G/A, GJA4 C/T, TCF7L2 C/T, ACE I/D, AGT M235T, AT1R A1166C, MTHFR C677T e MTHFR A1298C, 9P21 locus (rs1333049 G/C) and APOE (ε2, ε3, ε4). Data are presented by mean ± SD. Continuous variables are evaluated by Student t test and categorical variables by Chi Square tests. The power of the association was expressed by the Odds Ratio (OR) and 95% confidence intervals. Multivariate logistic regression is performed to determinate which polymorphic variants were significantly and independently associated with T2DM. A p-value less than 0.05 was considered statistically significant.
Results: The polymorphisms that showed association with T2DM, in the univariate analysis were: TCF7L2 TT (OR=1.69; p=0.0002) and AT1R CC (OR=1.58; p=0.021). After logistic regression, with all the genetic variants investigated and the environmental factors, only the TCF7L2 TT (OR=1.99; p<0.0001) remained in the equation showing to be significantly and independently associated with T2DM emergence.
Conclusions: This study suggests that there is in our population a genetic polymorphism that independently contributes to the development of T2DM. Since diabetes is associated with a very strong cardiovascular risk, the patients carrying this polymorphism should be approached with early preventive measures, in order to counteract their genetic tendency to develop diabetes.

P4286 | BEDSIDE
Insulin resistance is associated with similarly impaired LV myocardial deformation, untwisting and coronary flow reserve in first degree relatives and diabetic patients

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Insulin resistance is linked with endothelial dysfunction and arterial stiffness. In-