the 2013–2015 period. Patients with an interpretable EKG and a negative value of hsTnT for acute coronary syndrome (ACS) were included, all of them undergoing an early non-pharmacological treadmill stress test. Diagnostic precision was evaluated using a definite ACS diagnosis by independent cardiologists. Security was evaluated by presentation of intra-hospital events and in the follow-up.
Results: Of a total of 274 patients, 74 (27%) had an initial hsTnT value of <5ng/L. This group had a median age of 49 years, 44% of them being men with a low percentage of diabetics, and only 5% of them with previous history of ischemic cardiomyopathy.
A total of 65 (87%) negative and 9 (13%) positive stress tests were registered. In all positive cases a second diagnostic test was performed: 5 by a nuclear stress testing (SPECT) and 4 by a coronary angiogram, all of them turning out negative or without coronary lesions.
There was no final diagnosis for ACS, allowing calculating a 100% specificity value. No ACS, revascularization or death were registered in a 1-month follow-up in this group of patients, thus estimating a negative predictive value (NPV) of 100% for this cut point.
Conclusion: In our population, a single determination of hsTnT of <5ng/L shows a high specificity and high negative predictive value. Its implantation as a single rule-out test for chest pain should be prospectively examined in larger studies.

P3668 | BEDSIDE
Lesion characteristics and prognosis of heart attack without obstructive coronary artery disease

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Background: Patients with non-obstructive coronary artery disease are at high risk for cardiovascular mortality and morbidity. Detailed lesion characteristics are unclear.
Purpose: The aim of this study was to use optical coherence tomography (OCT) to investigate the lesion characteristics and prognosis of heart attack with non-obstructive coronary artery disease (NObHA).
Methods: This study consisted of 87 consecutive patients with NObHA who underwent OCT. Based on the presence of vulnerable lesions in the culprit artery, we classified the patients into a NObHA with vulnerable lesions (NObHA-VL) group and a NObHA without vulnerable lesions (NObHA-NL) group. A systematic clinical follow-up was performed at our outpatient clinic for up to 24 months. We defined cardiac death, myocardial infarction, and re-hospitalization for recurrent acute chest pain with obstructive coronary stenosis as a cardiac event.
Results: OCT revealed that 49 (56.3%) of 87 patients had hidden vulnerable lesions in the culprit artery, including ruptured plaque (19.5%), calcified nodule (10.3%), lone thrombus (9.2%), thin-cap fibroatheroma (TCFA; 8.0%), spontaneous coronary artery dissection (SCAD; 8.0%), and plaque erosion (1.1%). Of the patient characteristics recorded, only troponin elevation was different between the two groups (NObHA-VL 36.7% vs. NObHA-NL 13.2%, p=0.015). During angiography, 5 (10%) of 49 NObHA-VL patients complained of chest pain without ST change. Patients in the NObHA-VL group had poorer prognoses than those in the NObHA-NL group (p=0.042).
Conclusions: Hidden vulnerable lesions accompany NObHA, resulting in poorer outcomes. Vascular injury itself might provoke acute chest pain. OCT would be useful for the management of patients with NObHA.

P3669 | BENCH
Impaired cGMP and cAMP signaling in patients with coronary vasospasm: changes during acute crises

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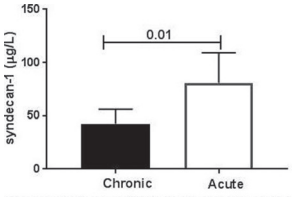
Background: Prinzmetal's angina (PA) and the coronary slow flow phenomenon (SCFP) are characterized by fluctuating severity of symptoms and a poor clinical response to treatment with sublingual nitrates. We have previously documented impaired cGMP and cAMP -based anti-aggregatory signaling in patients with unstable angina pectoris. To date, the status of these pathways in patients with PA/SCFP has not been investigated.
Purpose: We sought to measure platelet responsiveness to stimulation of cGMP (by the NO donor sodium nitroprusside: SNP) and of cAMP (by the prostacyclin [PGI2] analogue Iloprost) in patients with PA/CSFP, compared with that of age-matched controls. We also evaluated: (1) whether these parameters changed during acute exacerbations of symptoms and (2) whether there was activation of glycocalyx shedding (as a consequence of inflammatory activation) during chronic or acute phases of the disorder.
Methods: Venesection was performed in control subjects (n=22) and patients with either PA or CSFP during phases of acute symptomatic crises (n=6) or chronic symptomatic stability (n=24). Platelet responsiveness to SNP and Iloprost was determined via inhibition of ADP-induced aggregation in whole blood, using impedance aggregometry. Plasma concentrations of the glycocalyx component syndecan-1 (SD1) were measured by ELISA.
Results: Stable patients and control subjects were well-matched for age: the only significant differences between these groups being a higher proportion of patients who were smokers, or were being treated with calcium antagonists (p<0.05 for both). Data regarding comparisons between stable patients and controls are summarized in Table 1. During acute exacerbations, SD1 plasma concentrations were significantly higher, without further impairment of sGC- or AC-related responses (Figure 1).

Table 1

Parameter	Control (22)	Vasospastic angina (n=24)	P
ADP response (Ohms)	6.4 (0.36)	8.2 (0.49)	0.003
SNP response (% inhibition)	31.1 (4.1)	9.8 (2.1)	0.001
PGI2 response (% inhibition)	65.8 (6.7)	36.1 (6.3)	0.005
SD1 concentration (μg/L)	49.1 (1.9)	43.1 (5.2)	NS

Data in brackets are standard errors.



Plasma SD1 concentrations in chronic and acutely symptomatic vasospastic angina patients.
Figure 1

Conclusions: (1) Patients with coronary vasospasm have severely impaired platelet responsiveness to SNP and moderate impairment to Iloprost, even between symptomatic crises. (2) During acute symptomatic crises, there is activation of glycocalyx shedding, – potentially facilitating platelet-vessel wall interactions, – without further impairment of platelet responsiveness to SNP and Iloprost.
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P3670 | BEDSIDE
Efficacy and safety with ticagrelor in patients with prior myocardial infarction in the approved European label: insights from PEGASUS-TIMI 54

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Background: In PEGASUS-TIMI 54, ticagrelor significantly reduced the risk of the composite of major adverse cardiovascular events (MACE; CV death, MI or stroke) by 15–16% in stable patients with a prior MI 1–3 years earlier. The benefit of ticagrelor appeared more marked in patients continuing on or re-starting after only a brief interruption of ADP receptor inhibition and in those closer to their qualifying MI. The CHMP-EMA approved European label recommends that after the initial one-year treatment with ticagrelor 90 mg bd in ACS patients, treatment with ticagrelor 60 mg bd may be started without interruption as continuation therapy. Treatment can also be initiated up to 2 years from the MI, or within one year after stopping previous ADP receptor inhibitor treatment. We report the efficacy and bleeding safety in the PEGASUS subpopulation recommended for treatment in the European label.
Methods: PEGASUS-TIMI 54 randomized 21,162 patients who had had an MI 1–3 years earlier to ticagrelor at a dose of 90 or 60 mg, or placebo. 10,779 patients were ≤2 years from qualifying MI or ≤1 year from prior ADP receptor inhibitor treatment, 5388 in the ticagrelor 60 mg and 5391 in the placebo group. Hazard ratios, 95% confidence intervals and two-sided p-values were generated using the Cox proportional hazards model. The cumulative proportions of patients with events at 36 months were calculated by the Kaplan–Meier (KM) method.
Results: The composite of CV death, MI or stroke occurred in 373 patients (KM rate 7.9%) in the ticagrelor 60 mg group and in 463 patients (KM rate 9.6%) in the placebo group; HR 0.80 (95% CI 0.70, 0.91; p=0.001). Corresponding HRs for CV death, MI and stroke were 0.71 (0.56, 0.90; p=0.0041), 0.83 (0.70, 0.99; p=0.041) and 0.74 (0.55, 1.01; p=0.058), respectively. Ticagrelor also reduced the risk of all-cause mortality, HR 0.80 (0.67, 0.96; p=0.018). TIMI major bleeding occurred in 94 patients (KM rate 2.5%) in the ticagrelor group and in 43 patients (KM rate 1.1%) in the placebo group; HR 2.36 (1.65, 3.39, p<0.001). The corresponding HR for fatal or intracranial bleeding (n=27 ticagrelor vs 25 placebo) was 1.17 (0.68, 2.01; p=0.58).
Conclusion: In PEGASUS-TIMI 54, treatment with ticagrelor 60 mg in patients more recent to their MI or ADP receptor blocker discontinuation, as recommended in the European label, was associated with a relative risk reduction of 20% in CV death, MI or stroke, 29% in CV death, and 20% in all-cause mortality. Overall TIMI major bleeding was increased, but fatal or intracranial bleeding was similar

to placebo. There is a favorable benefit-risk ratio for long-term ticagrelor 60 mg in this population.

P3671 | BEDSIDE
Effectiveness of oral P2Y12 inhibition in men and women with cardiovascular disease: a meta-analysis and modelling study

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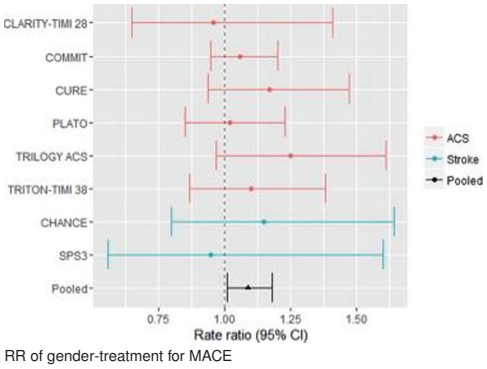
Background: The benefits and harms of oral P2Y12 inhibitors in women are not known, particularly for the newer P2Y12 inhibitors Prasugrel and Ticagrelor.
Methods: We performed a systematic review of randomised controlled trials of P2Y12 inhibitors and meta-analysed these data to produce gender-specific estimates of relative treatment efficacy for novel P2Y12 inhibitors (prasugrel and ticagrelor) in acute coronary syndrome and stroke. We subsequently combined these estimates with data on event rates in a Scottish population to estimate the absolute treatment effect using a Bayesian framework.
Results: From 7,148 articles identified through database searching, 36 potentially relevant articles were reviewed in detail. Of these, we identified 8 that fulfilled our inclusion criteria (CURE, COMMIT, CLARITY-TIMI 28, CHANCE, SPS3, TRITON-TIMI 38, PLATO and TRILOGY ACS). Overall, only 29.7% (32,561/109,570) of trial participants were women. The average gender-treatment interaction indicated lower efficacy for women than men. The rate ratio for interaction was 1.09 (95% CI 1.01–1.18).
Women experienced a larger risk of subsequent cardiovascular death following myocardial infarction (22.6% vs 14.8%) but bleeding deaths were similar (1.1% vs 0.8%) using age and sex-specific outcome data for men and women in Scotland. When the small relative difference in treatment effect was applied to data representative of the population, the absolute risk reduction in all-cause mortality at one-year was similar in both sexes (2.30%; 95% CI 1.51 to 3.05 and 2.06%; 95% CI 0.29 to 3.73 in men and women respectively).



RR of gender-treatment for MACE

Conclusion: In a meta-analysis and modelling study using data from 100,000 participants randomised to P2Y12-inhibitors and over 45,000 patients from the Scottish population hospitalized we have identified that newer P2Y12 inhibitors are less efficacious in women than men (around 1.1-fold lower), but that the absolute risk reduction is similar in both sexes.

P3672 | BEDSIDE
High-sensitivity troponin: the challenge of improving classification and prognostic stratification of NSTE-ACS

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Background: The introduction of novel high sensitivity assays for cardiac troponin (hs-cTnT), able to detect very low circulating troponin level, has thouroughly influenced both the diagnostic and the prognostic assessment of patients with non-ST-segment elevation acute coronary syndromes (NSTE-ACS).
Purpose: We assessed the additional diagnostic value of a hs-cTnT assay (Elecsys Troponin T high-sensitive assay, Roche Diagnostics) and its ability to predict adverse outcomes in the setting of non-ST-segment elevation acute coronary syndromes (NSTE-ACS).
Methods: We studied 644 patients with unstable angina (IIIB class, Braunwald classification) enrolled in a a multicentre prospective study, named SPAI (Stratificazione Prognostica nell'Angina Instabile). Patients with myocardial infarctions (MI) according to WHO definition were excluded. The study's primary endpoint was the composite of death and non-fatal MI at 180 days of follow-up. New hospitalization for unstable angina during the follow-up period defined the secondary endpoint.
Results: The adoption of hs-TnT cut-off value ≥99th percentile (14 ng/L) identified 404 (62.7%) "new" MIs. Hencesoforth, about one third of the unstable angina episodes, diagnosed by previous-generation troponin assay, clinically used at the time of patients' recruitment, became NSTEMIs with the introduction of the high sensitivity assay. Our analysis confirmed the independent prognostic role of cardiac troponin: the rate of primary endpoint significantly increased across higher hs-TnT quartiles at 30 days (p 0.0033) as well as at 180 days (p 0.0069) of follow-up. Furthermore, the rate of death/non-fatal MI at 180 days was higher in patients with hs-TnT≥99th compared to those with negative levels of hs-TnT (11.1% vs 4.6%, HR 2.42, 95% CI 1.3–4.9; log-rank p 0.004). However, hs-TnT measurements did not add prognostic information on the secondary endpoint. Conversely, a score (Instability Score - IS), based on the occurrence of previous history of unstable angina and/or persistence of instability at 48 hours after admission (IS-1 and IS-2, respectively) resulted to be associated with a higher risk of recurrent unstable angina during the follow-up period (IS-1 HR 1.76, 95% CI 1.07–2.91, p 0.0266; IS-2 HR 3.49, 95% CI 1.72–6.63, p<0.001).
Conclusion: The major diagnostic ability of hs-TnT at the 99th percentile compared to the conventional cTn assays allows for the prediction of adverse events in patients with NSTE-ACS. Furthermore, the absence of a direct correlation between hs-TnT levels and recurrence of instability at follow-up supports the concept that it cannot be considered as a biomarker that "fits for all".

P3673 | BEDSIDE
Differences in mortality between patients referred to coronary angiography with stable angina or unstable angina

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Introduction: New, high-sensitivity troponins detects very small amounts of myocardial necrosis, uncovering myocardial infarctions in patients previously diagnosed with unstable angina (UA). Consequently, the mortality and morbidity in the UA population is falling, leading some to suggest that the diagnosis of UA will become redundant in the future. The difference in mortality between patients presenting with UA and stable angina remains unclear.
Purpose: To investigate differences in mortality between patients presenting to coronary angiography (CAG) as UA and stable angina.
Methods: Study participants were recruited from the clinical registry of all CAGs performed at the sole providing hospital in the region. We included all procedures

Abstract P3671 – Trials included in meta-analysis

Trial, year	n	Population	Drug/comparator	Dosage	Duration of treatment	Follow-Up
CURE, 2001	12,562	Patients presenting to hospital with acute coronary syndrome within 24 hours after onset of symptoms and did not have ST elevation	Clopidogrel/placebo	300mg loading dose followed by 75mg once daily	3 to 12 months (mean duration of treatment, 9 months)	12 months
COMMIT, 2005	45,852	Patients admitted within 24 hours of suspected acute MI onset with ST elevation, left-bundle branch block, or ST depression.	Clopidogrel/placebo	75mg	Hospital discharge or 28 days. (mean 14.9 days)	Hospital discharge or 28 days.
CLARITY-TIMI 28, 2005	3,491	Patients 18 to 75 years of age presenting within 12 hours after onset of STEMI	Clopidogrel/placebo	300mg loading dose followed by 75mg once daily	Up to day of Coronary Angiography, day 8 or hospital discharge	30 days
TRITON-TIMI 38, 2007	13,608	Patients with acute coronary syndrome with scheduled PCI	Prasugrel/clopidogrel	60mg loading dose followed by 10mg once daily	6 to 15 months (median, 14.5 months)	15 months
PLATO, 2009	18,624	Patients hospitalized for an acute coronary syndrome with an onset of symptoms during previous 24 hours	Ticagrelor/clopidogrel	180mg loading dose followed by 90mg twice daily	12 months	12 months
CHANCE, 2010	5,170	Patients within 24 hours after the onset of minor ischemic stroke or high-risk TIA	Clopidogrel/placebo	300mg loading dose followed by 75mg once daily	90 days	90 days
TRILOGY ACS, 2012	72,43	Patients with unstable angina or NSTEMI selected for medical management without revascularization within 10 days after the index event	Prasugrel/clopidogrel	30mg loading dose followed by 10mg once daily	30 months	30 months
SPS3, 2012	3,020	Patients with recent symptomatic lacunar infarcts identified by magnetic resonance imaging.	Clopidogrel/placebo	75mg	3.4 years	3.4 years