predictors of major bleeding in normotensive patients only. Haemodynamic instability was associated with 2.07-fold increased risk for major bleeding (1.26–3.38, p=0.004).

	Haemodynamic unstable (n=190)			Normotensive (n=365)	
	OR (95% CI)	n/N (%)	p-value*	n/N (%)	OR (95% CI)
Age >75 years	1.87 (0.91-3.88)	69/189 (37)	**0.005**	96/363 (26)	1.15 (0.55-2.42)
Female sex	1.30 (0.62-2.71)	108/189 (57)	0.088	184/365 (50)	**2.66 (1.28-5.54)**
Previous surgery (within 4 weeks)	**3.46 (1.35-8.88)**	22/190 (12)	**0.017**	20/364 (5.5)	2.28 (0.72-7.21)
Cancer	0.62 (0.20-1.89)	29/189 (15)	**0.014**	30/363 (8.3)	0.59 (0.14-2.58)
Anaemia†	**3.18 (1.49-6.75)**	70/181 (39)	**<0.001**	64/313 (20)	**2.51 (1.12-5.28)**
Syncope	1.35 (0.65-2.79)	87/186 (47)	**<0.001**	89/365 (24)	**2.53 (1.26-5.07)**
GFR <30 ml/min/1.73m²	**2.51 (1.01-6.23)**	26/181 (14)	**0.002**	21/348 (6.0)	2.10 (0.67-6.60)
Platelet count ≤100,000/µl	1.42 (0.36-5.53)	12/180 (6.7)	0.076	11/342 (3.2)	1.88 (0.39-9.05)
ASA	0.78 (0.24-2.47)	27/147 (18)	**0.009**	29/303 (9.6)	1.93 (0.61-6.06)

* p-value for two-tailed Fishers exact test.

†defined as Hb <13 g/dl in males and <12 g/dl in females.

Predictors of major bleeding

Conclusion: In this large pooled European multicentre "real-world" cohort of thrombolysed PE patients, the prevalence of risk factors for major bleeding and their prognostic impact differed in haemodynamic unstable compared to normotensive patients. If considering thrombolysis in normotensive PE patients, the risk of major bleeding related to anaemia, female sex and syncope might deserve more attention.

SEX-RELATED DIFFERENCES IN THE OUTCOMES OF CARDIOVASCULAR INTERVENTIONS

2165
Temporal trends in sex-related differences in clinical characteristics and outcome of patients undergoing transcatheter aortic valve implantation - data from a national TAVI registry

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Background: Cumulative findings from various worldwide cohorts have shown sex-related differences in patients undergoing transcatheter aortic valve implantation (TAVI), yet data regarding the effect of TAVI evolution on sex-related differences are limited.

Aims: To evaluate temporal trends in sex-related differences regarding demographic and echocardiographic characteristics, procedural and long-term outcome in patients undergoing TAVI.

Method: We evaluated patients who underwent TAVI for severe symptomatic aortic stenosis from a national TAVI registry including four tertiary hospitals between the years 2008–2016.

Results: Our final cohort included 1,358 female and 1,149 male patients. During 2008–2012, VARC-2 defined procedural success and procedural morality were comparable between male and female patients. However, male patients had an increased risk of significant para-valvular leak (p<0.001), pacemaker implantation (p=0.002) and stroke (p=0.004) compared to female patients. During 2013–2016, procedural mortality was higher in female patients compared to male patients, though VARC-2 defined procedural success rates were similar. Male and female patients exhibited similar rates of significant para-valvular leak, pacemaker implantation and stroke (p>0.1 for all comparisons). The cumulative incidence of death through 3 years of follow-up was significantly lower in female patients than in male patients during years 2008–2012, but not during years 2013–2016 (Figure). Multivariate analyses showed that female patients who underwent TAVI between years 2008–2012 had 26% lower risk of death compared to male patients (p=0.004), but there were no sex-related differences in mortality risk between the years 2013–2016 (HR=1.07, p=0.6, gender-by-year of procedure, p for interaction = 0.027).

Conclusion: Female patients undergoing TAVI present with distinct baseline and procedure-related characteristics which may impact procedure related complications and long term outcome. Improved prognosis was observed among female versus male patients in the early TAVI period, but outcomes seem to balance in the current period.

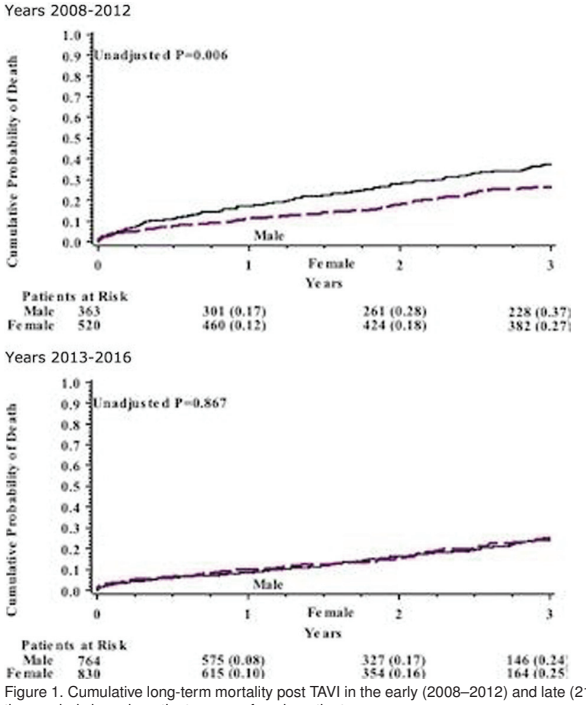

Figure 1. Cumulative long-term mortality post TAVI in the early (2008–2012) and late (213–2016) time periods in male patients versus female patients.

2166
STEMI in women undergoing primary PCI: time to make a (gender) difference

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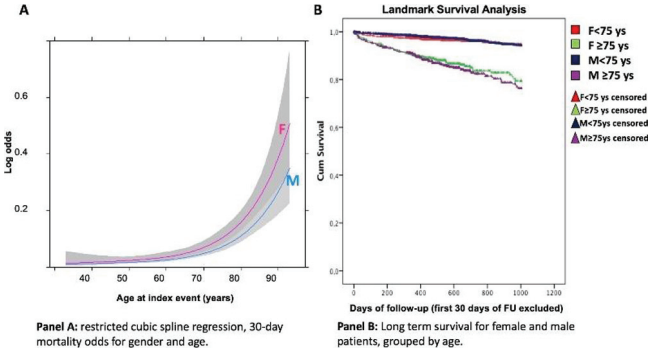
Background: Since female patients usually present at later age at first myocardial infarction event, the role of gender on clinical outcomes is controversial.

Purpose: The purpose of our analysis is to investigate the effects of gender on mortality in patients with ST-Elevation Myocardial Infarction (STEMI) undergoing primary PCI (pPCI).

Methods: We enrolled 4365 consecutive STEMI patients treated with pPCI between 2006 and 2017 at two Italian centres. The primary endpoint was mortality at 30 days. The secondary endpoint was mortality at follow up. Patients according to their gender were compared using Fisher's exact test and Mann-Whitney test as appropriate. Logistic regression analysis was used to predict the role of gender and age in determining 30-day mortality. Mortality outcomes were estimated using Kaplan-Meier curves with log-rank test.

Results: The mean age of the overall population was 64.4 years ± 12.8. Women were 24.6% (n=1073), older (70.4 vs. 62.4 years, p<0.0001), more likely to be hypertensive (67.6% vs.52.2%, p<0.0001), diabetic (22.3% vs. 18.5%, p=0.007), less likely to be smokers (37% vs. 59.2%, p<0.0001), less likely to have had a previous MI (8.9% vs. 11.8%, p=0.008), more likely to have single vessel disease (52.7% vs 47.4%, p<0.0001) and more likely to have Killip class>2 at presentation (19.3% vs. 12.5%, p<0.0001). Women also had lower haemoglobin values at admission (13 vs 14.5 g/dL, p<0.0001). Mortality at 30 days was 5.8% in the overall population: 4.3% and 10.2% of the male and female sample, respectively. The odds ratio for mortality at 30 days for female patients was 1.5 (95% CI 1.12–1.96, p=0.006) and 1.08 for every year of age in the overall population (95% CI



Panel A: restricted cubic spline regression, 30-day mortality odds for gender and age.

Panel B: Long term survival for female and male patients, grouped by age.

Figure 1

1.06–1.09, p<0.0001). The relationship between short-term mortality and gender held especially true for elderly patients (see restricted cubic spline regression graph below, Panel A). However, gender was not an independent predictor of long-term mortality, as shown (figure below, Panel B) by the landmark survival analysis (in which we excluded the events in the first 30 days of follow-up), with superimposable survival curves among men and women, grouped by age.
Conclusions: Our analysis showed an independent role of gender in determining short-term mortality in STEMI patients undergoing primary PCI, with a significantly increased risk for women compared to men. On the other hand, when considering long-term mortality, gender did not affect the outcome; the variable that made the survival curves diverge was age. The observed gender difference in mortality in the very first period after an acute myocardial infarction warrants further focused investigation to better define underlying causes.

2167
Influence of gender on long-term prognosis in patients with atrial fibrillation treated with oral anticoagulants. Results from the prospective, nationwide FANTASIIA study

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Background and aims: Several well known clinical features and embolic and bleeding scores have demonstrated to be markers of prognosis in patients with atrial fibrillation (AF). The aim of our study was to investigate the role of gender as a long-term predictor of prognosis in "real world" patients with AF treated with direct oral anticoagulants (DOAC) or vitamin K antagonists (VKA) in a nationwide observational study.
Methods: The FANTASIIA study prospectively included outpatients with AF treated with DOAC or VKA, consecutively recruited from June 2013 to October 2014 in 50 Spanish centers. Basal features and embolic events, severe bleedings and all-cause and cardiovascular mortality rates up to 3 years of follow-up were analyzed, and a Cox multivariate analysis was performed to investigate the role of gender in predicting major events.
Results: A total of 2177 patients were included in the study, with a mean age of 73.8±9.4 years, being male 56.2% and female 43.8%. Of these 2177 patients, 533 (24.5%) received DOAC and 1944 (75.5%) VKA (without differences by gender), 80.5% had hypertension, 29.6% diabetes, 17.1% previous stroke, 18.9% renal failure, 28.5% heart failure, 18.1% coronary heart disease, and 3.9% previous severe bleedings. Mean CHA2DS2-VASc was 3.7±1.6 and HAS-BLED 2.0±1.0. After up to 3 years of follow-up, 5005.45 patients/year of observations accumulated. Rates of major events (female versus male, patients/year) were: stroke: 0.77 vs 1.01 (p=0.38), total embolisms: 0.77 vs 1.12 (p=0.21), severe bleedings 2.91 vs 3.07 (p=0.74), embolisms and/or severe bleedings: 3.63 vs 4.07 (p=0.44), cardiovascular death: 2.3 vs 2.01 (p=0.48), total death: 4.42 vs 5,63 (p=0.06), and that of the combined event stroke/severe bleeding/total death: 6.99 vs 8.78 (p=0.029). After adjusting for baseline confounding factors in a Cox multivariate analysis, females showed, in comparison with male patients, similar rates of cardiovascular death (HR 0.89, 0.59–1,34), and lower rates of total death (HR 0.62, 0.47–0.81, p<0.001), embolisms and/or severe bleedings (HR 0.73, 0.54–0.99, p=0.041), embolism/severe bleeding/total death (HR 0.64, 0.52–0.80, p<0.001) and embolism/severe bleeding/cardiovascular death (HR: 0.76, 0.59–0.99, p=0.039), as well as a trend to lower rates of stroke (HR: 0.63, 0.34–1.16. p=0.1), total embolisms (HR 0.57, 0.31–1.03, p=0.06) and severe bleedings (HR 0.78, 0.56–1.10, p=0.1).
Conclusion: In this nationwide, "real world", prospective study of patients with AF receiving oral anticoagulation, female gender seems to play a protective role against the development of major cardiovascular events, mainly on total death and combined events including embolisms and bleedings.
Funding Acknowledgements: Unrestricted grant from Pfizer Spain

SOMETHING OLD, SOMETHING NEW: BIOMARKERS AND CARDIOVASCULAR RISK ASSESSMENT

2170
Screening multiple biomarkers for associations with cardiovascular death in patients with stable coronary heart disease

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Background: Risk assessment of future major adverse events in patients with stable coronary heart disease (CHD) is usually based on clinical risk factors. However, the precision in predicting events in these patients is low. In other diseases, novel biomarkers have shown to enhance risk prediction.
Purpose: To investigate if the associations between 155 potential protein biomarkers and cardiovascular death (CVD), improve risk assessment of patients with stable CHD on optimal secondary prevention therapy, in addition to established biomarkers and clinical risk factors.
Methods: In the Stabilization of Atherosclerotic Plaque by Initiation of Darapladib Therapy (STABILITY) trial, 15,828 patients with stable CHD and at least one clinical risk factor were included. During a median follow-up time of 3.7 years, 605 patients had CVD. Baseline plasma samples from all cases with CVD and 2,789 randomly selected control cases from the same cohort, underwent analysis for normalized protein expression (NPX) levels with proximity extension assay (PEA) technology. An unbiased selection of variables with CVD association (proteins and clinical risk factors) was performed with random forest analysis. Confirmation of variable importance for CVD was determined by Boruta analysis. Independent association between variables and CVD was evaluated by weighted multivariate Cox regression analysis adjusted for baseline characteristic and established cardiorenal biomarkers: cystatin C, N-terminal prohormone of brain natriuretic peptide (NT-proBNP) and high sensitivity troponin T (hs-TnT). Cox regression analysis used NPX levels modeled as continuous by standard deviation and because of multiple testing, threshold of significance was Bonferroni adjusted (p<0.00039).
Results: Median age was 69 years for cases and 65 years for controls. At baseline 92% and 97% were treated with acetylsalicylic acid and statin, respectively. Out of 155 analyzed proteins, 85 differed in NPX levels when comparing cases and controls (p<0.0001). After selection of variables associated with CVD, variable importance was confirmed for 28 proteins. Further, 4 of them passed the threshold of significance with independent associations (hazard ratio, 95% confidence interval) with CVD in adjusted models comparing cases with controls: NT-proBNP 2.35 (2.05–2.69), hs-TnT 1.48 (1.32–1.66), TRAIL receptor 2 (TRAIL-R2) 1.25 (1.15–1.35) and hepatocyte growth factor (HGF) 1.22 (1.10–1.36).
Conclusions: In this well-managed cohort of patients with stable CHD and high cardiovascular risk, the established cardiac risk markers NT-proBNP and hs-TnT were independently associated with CVD. The novel biomarkers TRAIL-R2 and HGF added prognostic value beyond that of conventional variables but need further validation. Furthermore, there was a sizable number of potential protein biomarkers associated with outcome before adjustment for established cardiorenal biomarkers, which need further evaluation.
Funding Acknowledgements: GlaxoSmithKline, Swedish Foundation for Strategic Research, Roche

2171
Cardiovascular preoperative screening system for non-cardiac surgery modified from ACC/AHA guideline can provide effective evaluation

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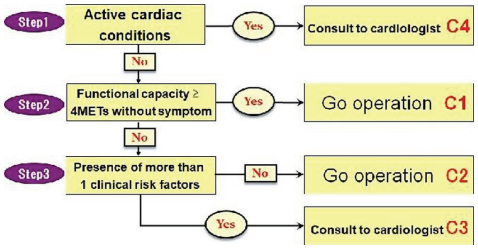
Background: We developed new cardiovascular screening system named as "Cardiac Preoperative Screening (CPS)" before non-cardiac surgery modified from ACC/AHA 2007 and ESC/ESA 2014 Guidelines.
Purpose: The purpose of this study was to evaluate the usefulness of this system and the incidence of cardiac events under CPS system during perioperative period.
Methods: This study included a total of 12,841 consecutive patients (5,788 male, age 57±17 y/o) who underwent planned adult non-cardiac surgery in our hospital from October 2013 to June 2016. Patients answered the interview 1 month before surgery about the presence of active cardiac diseases, exercise capacity and clinical risk factors. Patients were classified into 4 categories; C1 to C4; C1 (above 4METs without cardiac symptom), C2 (less than 4METs without clinical risk factors), C3 (less than 4METs and at least 1 clinical risk factor) and C4 (with unstable symptoms). In this system, the patients in C1 and C2, are classified to Operation group, undergo surgery directly, and patients in C3 and C4, "Consultation group", should be consulted to cardiologist before surgery.
Results: Of 12,841 cases, CPS was performed in 11,161 cases (86.9%), C1: 10,081, C2: 423, C3: 364, C4: 293 cases. Out of these, 1,407 cases (12.6%) were consulted to cardiologist before surgery. Among these, cardiac events developed in 151cases (1.4%), including 27 ischemic coronary events (0.24%); 8 vasospastic angina, 7 acute myocardial infarction, and 12 unstable angina. The event-rate of all cardiac events was higher in Consultation group than in Operation



CPS screening chart