Univariate analysis suggested a significant reduction of MACCE only in Group B (OR 0.25, 95% CI: 0.08–0.83, p=0.02) when compared to Group A. When adjusted for age, sex, clinical syndrome and primary PCI status this finding remained statistically significant in multivariate analysis (OR 0.27, 95% CI 0.08–0.90, p=0.03). Kaplan-Meier log-rank analysis (see Figure) through to 360-days demonstrated no statistical difference in DAPT regime on MACCE (long-rank test, p=0.116).
Group A experienced the highest bleeding rates, followed by Groups B and C (see Figure). Multivariate logistic regression identified age>75 years as an independent predictor of bleeding (OR 2.05, 95% CI: 1.22–3.44, p<0.01).
Conclusion: In our observational analysis of an unselected cohort, ticagrelor use was associated with an overall reduction in MACCE. However, there was no significant difference in adverse events between different DAPT regimes at 1 year. Furthermore, our analysis suggests that newer antiplatelet agents (Ticagrelor and Prasugrel) are non-inferior to Clopidogrel in their risk of bleeding, contrary to the common belief of many physicians. Our study highlights the need for further large-scale prospective real-world analyses to investigate predictors of MACCE and bleeding and identify the groups that are most likely to benefit from newer DAPT regimes, for a tailored approach to patient-centred care.

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Association of plasma concentration of trimethylamine N-oxide and ADP-induced platelet reactivity after a loading dose of clopidogrel 600 mg in patients undergoing elective PCI

C. Stratz[1], A. Gessner[2], M.F. Fromm[2], J. Hromek[1], T. Nuehrenberg[3], L. Hille[1], F.-J. Neumann[3], W. Hochholzer[3], D. Trenk[1]. *[1]University Heart Centre Freiburg – Bad Krozingen, Clinical Pharmacology, Bad Krozingen, Germany; [2]University of Erlangen-Nuremberg, Institute of Experimental and Clinical Pharmacology and Toxicology, Erlangen, Germany; [3]University Heart Center Freiburg-Bad Krozingen, Dept. Cardiology and Angiology II, Bad Krozingen, Germany*

Background: Exposure to trimethylamine N-oxide (TMAO) has been associated with an increased risk for cardiovascular events. It has been shown that elevated TMAO concentrations are predictive for an incident risk for thrombotic events with TMAO increasing platelet hyperreactivity and thrombosis potential as suggested mechanisms. At present, there is no data available if TMAO impacts on antiplatelet efficacy of the P2Y12 receptor antagonist clopidogrel.
Objectives: We investigated association of TMAO plasma concentrations and adenosine diphosphate (ADP)-induced platelet reactivity (PR) after a loading dose of clopidogrel 600 mg.
Methods: This sub-study of the EXCELSIOR trial comprised 760 patients with stable coronary artery disease undergoing percutaneous coronary intervention with stent implantation (PCI). Platelet reactivity was assessed by light-transmission aggregometry after stimulation of platelet rich plasma with ADP (5 μmol/l), before (intrinsic) as well as at the day after a loading dose of clopidogrel 600mg and administration of the first maintenance dose (75mg). Plasma TMAO levels were determined by stable isotope dilution liquid chromatography with online tandem mass spectrometry. CYP2C19 genotype, which is a major determinant of clopidogrel bioactivation, was analyzed by real-time PCR.
Results: Reliable TMAO plasma concentrations could be determined in all samples. Intrinsic PR showed no significant correlation with TMAO levels (Spearman's r=0.057, p=0.114). At day 1 after PCI, a somewhat closer association between TMAO plasma levels and platelet reactivity was observed for the entire group (r=0.107; p=0.003). The association was improved further if the analysis was restricted to CYP2C19 wild-type patients (n=527; r=0.135; p=0.002). We calculated a cut-off plasma concentration of 4.6 μmol/L TMAO by ROC analysis and Youden-Index for high on-treatment PR (>14% ADP-induced aggregation). Thereafter, univariate (OR 1.7 [CI: 1.2–2.4], p<0.001) and multivariate analysis (OR 1.6 [CI: 1.1–2.3], p=0.01) yielded predictive values for elevated TMAO levels on high PR.
Conclusions: A statistically significant association between elevated TMAO levels and high on-treatment platelet reactivity was observed in patients on treatment with clopidogrel. Thus, our results demonstrate for the first time that TMAO plasma concentration seems to be another piece in the puzzle of variables contributing to the variability in antiplatelet response to clopidogrel.

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Meta-analysis of use of proton pump inhibitors with dual antiplatelet therapy after acute coronary syndrome

A. Lone[1], S. Khan[1], H. Riaz[2], I.B. Riaz[3], E. Kaluski[1]. *[1]Guthrie Clinic, Internal Medicine, Sayre, PA, United States of America; [2]Cleveland Clinic Foundation, Cleveland, United States of America; [3]Mayo Clinic, Rochester, United States of America*

Background: Professional guidelines recommend the use of proton pump inhibitors (PPI) with dual antiplatelet therapy (DAPT) to reduce the risk of gastrointestinal (GI) bleeding. However, there is a disconnect between guidelines and clinical practice regarding the use of PPI.
Purpose: To compare the effects of PPI versus no PPI in patients receiving DAPT after acute coronary syndrome (ACS)
Methods: 39 studies were selected using MEDLINE, EMBASE and CENTRAL (Inception-November 2017). Estimated were pooled using generic invariance weighted random effects model.
Results: In analysis of 255,197 patients (PPI=90,917 patients and no PPI = 164,280 patients), the use of PPI was associated with 28% relative risk increase in all-cause mortality compared with no PPI (Relative risk (RR), 1.28, 95% confidence interval (CI), 1.13–1.44, P<0.001) and 25% risk increase in cardiovascular mortality (RR, 1.25, 95% CI, 1.04–1.51, P=0.02). The use of PPI increased the risk of myocardial infarction (RR, 1.33, 95% CI, 1.19 -1.49, P<0.001), revascularization (RR, 1.26, 95% CI, 1.04–1.53, P=0.02), stent thrombosis (RR, 1.32, 95% CI, 1.16–1.50, P<0.001) and stroke (RR, 1.60, 95% CI, 1.43–1.78, P<0.001). The use of PPI had no beneficial effect on preventing the risk of total bleeding events (RR, 1.12, 95% CI, 0.95–1.33, P=0.18) or GI bleeding (RR, 0.65, 95% CI, 0.39–1.08, P=0.10).

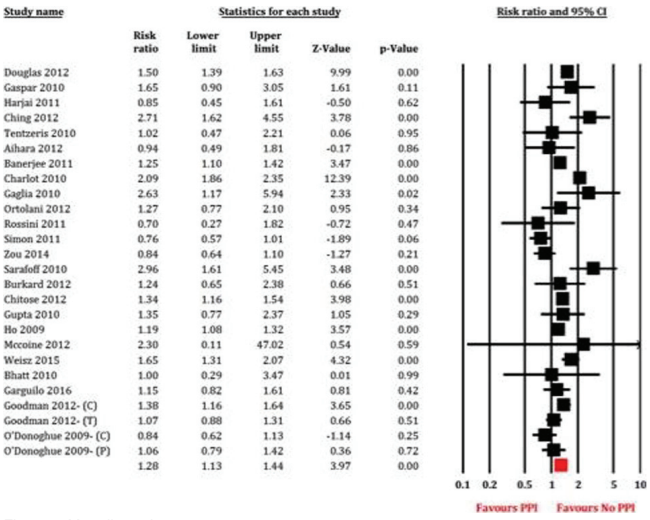

Figure 1. Mortality estimate

Conclusion: In patients after ACS, the use of PPI with DAPT did not prevent GI bleeding, rather the concomitant use of PPI with DAPT was associated with increased risk of mortality and cardiovascular outcomes.

ATRIAL FIBRILLATION IN HEART FAILURE

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Prognostic implications of atrial fibrillation in heart failure with reduced, mid-range, and preserved ejection fraction: a report from 14,964 patients in the ESC heart failure long-term registry

B. Zafrir[1], L.H. Lund[2], C. Laroche[3], F. Ruschitzka[4], M.G. Crespo-Leiro[5], A.J.S. Coats[6], S.D. Anker[7], G. Filippatos[8], P. Seferovic[9], A.P. Maggioni[10], O. Amir[11]. *[1]Lady Davis Carmel Medical Center, Cardiology Department, Haifa, Israel; [2]Karolinska Institute, Department of Medicine, Karolinska Institutet, and Heart and Vascular Theme, Karolinska Hospital, Stockholm, Sweden; [3]EURObservational Research Programme, European Society of Cardiology, Sophia Antipolis, France; [4]University Hospital Zurich, Department of Cardiology at the University Hospital in Zürich, Switzerland, Zurich, Switzerland; [5]University Hospital A Coruna, Unidad de Insuficiencia Cardiaca Avanzada y Trasplante Cardiaco, Corunna, Spain; [6]University of Warwick, Coventry, United Kingdom; [7]University Medical Center Gottingen (UMG), Innovative Clinical Trials, Department of Cardiology & Pneumology, Gottingen, Germany; [8]University Hospital 12 de Octubre, Cardiology Department, Madrid, Spain; [9]Clinical center of Serbia, Department of Cardiology, Belgrade, Serbia; [10]Associazione Nazionale Medici Cardiologi Ospedalieri Research Center, Florence, Italy; [11]Baruch Padeh Medical Center, Cardiovascular Department, Tiberias, Israel.*
On behalf of the ESC-HFA Heart Failure Long-Term Registry Investigators

Background: Atrial fibrillation (AF) associated with poor prognosis in heart failure (HF) but whether this differs by ejection fraction (EF) is poorly understood.
Methods: Data from the observational, prospective, HF long-term registry of the Heart Failure Association (HFA) of the ESC was analyzed to compare the characteristics and 1-year prognostic role of AF between HF with reduced (HFrEF<40%), mid-range (HFmrEF 40–49%) and preserved (HFpEF≥50%) ejection fraction.
Results: A total of 14,964 HF patients (age 66±13 years; 67% males, 53% HFrEF, 21% HFmrEF, 26% HFpEF) were enrolled. The prevalence of AF was 26% in HFrEF, 29% in HFmrEF and 39% in HFpEF. AF was associated with older age, reduced functional capacity and more physical signs of HF. Crude rates of mortality and HF hospitalization were higher in patients with AF compared to sinus rhythm, in each EF group. After multivariable adjustment, the 1-year hazard ratio of AF for all-cause death was 0.922 (95% CI 0.782–1.087, p=0.334), 1.136 (95% CI 0.878–1.470, p=0.332) and 1.245 (95% CI 1.002–1.546, p=0.048), for HFrEF, HFmrEF and HFpEF, respectively, and for HF hospitalizations: 0.948 (95% CI 0.817–1.100, p=0.480), 1.518 (95% CI 1.157–1.99, p=0.003) and 1.401 (95% CI 1.151–1.706, p<0.001), respectively. Moreover, in both acute and chronic HF pre-