sis in the setting of the increased platelet turnover that occurs post-operatively, we performed a randomized trial to determine whether higher-dose once-daily or more frequent ASA dosing overcomes the resistance observed with usual ASA dosing.
Methods: Adults undergoing CABG surgery were randomized to one of 3 ASA dosing regimens; 81 mg once-daily, 325 mg once-daily, or 81mg four times daily. ASA was started on the first post-operative day and continued until day 7 or hospital discharge. Using an immunoassay, levels of serum TXB2, the stable metabolite of TXA2, were measured daily before starting ASA. The primary outcome was the median TXB2 level on postoperative day 4.
Results: A total of 100 patients undergoing CABG surgery (mean age 65, females 16%) were randomized. On day 4, median TXB2 level in the group receiving ASA 81mg once-daily was 10.7 ng/ml (Q1,Q3; 6.1,30.8 ng/ml). The median TXB2 levels were significantly lower in the groups randomized to ASA 325 mg once-daily and 81 mg four times daily; 3.6 ng/ml (Q1,Q3; 1.9,10.1 ng/ml) and 1.1 ng/ml (Q1,Q3; 0.5,2.4 ng/ml), respectively; P=0.001 and P<0.0001, respectively.
Conclusions: ASA resistance after CABG surgery, defined as failure of ASA to suppress TXB2 formation, is attenuated by higher dose once-daily ASA and almost abolished by four times daily low-dose ASA. The efficacy of more frequent ASA dosing supports the concept that resistance reflects, at least in part, increased platelet turnover. Attenuation of TXB2 production by higher dose once-daily ASA raises the possibility that the susceptibility of megakaryocyte COX-1 to acetylation by ASA may be dose-dependent.

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The risk for stent thrombosis after discontinuation of clopidogrel for PCI patients waiting for surgery

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Purpose: A treatment dilemma currently exists in patients receiving P2Y12 inhibitors for coronary artery disease who require surgery. Product labels for P2Y12 inhibitors include a warning for thrombotic cardiac events after premature discontinuation. However, the same labels, as well as treatment guidelines, recommend to discontinue P2Y12 inhibitors 5-7 days before surgery.
Premature clopidogrel discontinuation is the most pronounced risk factor for stent thrombosis (ST), and therefore, patients awaiting surgery who discontinued clopidogrel may be at increased risk for ST. However, the absolute risk of ST is unknown. This study aimed to determine the absolute risk of ST in PCI patients who premature discontinue clopidogrel and to evaluate the risk of ST post discontinuation as a function of time and duration after PCI.
Methods: Reanalysis of a ST Registry including all ST patients (cases, n=437) and control patients (n=866) as part of an all-comer PCI Registry (n=21,009) was performed to determine the 1) absolute risk of ST by extrapolation of clopidogrel discontinuation rates from the ST Registry to PCI Registry, 2) risk of ST as a function of time (≤7, 8-14, 15-30 days) post discontinuation, and 3) risk of ST as a function of duration of clopidogrel therapy ≤30, ≤180 days after PCI. Clopidogrel discontinuation was variable at that time in the Netherlands, mostly because health insurance companies reimbursed anywhere between 1-12 months.
Results: Clopidogrel was discontinued in 30.7% and 13.5% of the cases and controls. Of cases 37.3%, 15.7%, and 6.0% experienced ST within 7, 8-14, and 15-30 days post discontinuation. The relative risk was highest ≤7 days post discontinuation (HR 36.8; 14.6-92.4) vs. 8-14 (HR 34.9; 7.5-162.7) and 15-30 days (HR 17.7; 1.8-169.2), also after adjusting for confounding factors (adjusted HR ≤7 vs. 8-14 days: HR 53.2; 7.5-377.5; HR 29.2; 3.45-247.3). The relative risk ≤7 days post discontinuation was similar when ST occurred within 30 or 180 days after PCI (HR 33.2; 8.4-131.9; HR 28.2; 9.3-85.7). Further, the absolute risk of ST within 7 days post discontinuation was importantly increased when it occurred within ≤30, and 31-180 days after index PCI compared 181-365 days after PCI (absolute risk: 41.0%; 25.2%; 5.9%).
Conclusion: Patients who premature discontinue clopidogrel are at risk for ST within 7 days post discontinuation, in particular within 180 days after index PCI. For patients awaiting surgery within 180 days after PCI, it might be optional to reduce this risk by using a rapid reversible platelet inhibitor to sustain P2Y12 inhibition until surgery.

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The predictors of discharge without clopidogrel following admission with acute coronary syndrome in australia - the concordance registry

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Purpose: There is strong evidence for the use of ADP receptor blockade (clopidogrel) in secondary prevention. This analysis determined predictors of failure to discharge patients on clopidogrel following an ACS.
Methods: Demographic and clinical data were collected for the CONCORDANCE registry from 23 hospitals around Australia. Multivariate logistic regression was used to determine the independent predictors of discharge without clopidogrel.
Results: Among patients surviving to discharge with a diagnosis of ACS, 33.2% were not discharged on clopidogrel. This figure was higher in medically managed patients (38.3%) In 30.3% of patients who received clopidogrel in hospital, the drug was stopped at discharge. Predictors of discharge without clopidogrel were: unstable angina (OR 0.67, 95% CI 0.51 to 0.88) (referent myocardial infarction), coronary artery bypass grafting (OR 0.075, 95% CI 0.051 to 0.11) and discharge with warfarin (OR 0.28, 95% CI 0.20 to 0.39).
In patients receiving clopidogrel in hospital, the independent predictors of discharge without clopidogrel remained the same: unstable angina (OR 0.50, 95% CI 0.34 to 0.72), coronary artery bypass grafting (OR 0.06, 95% CI 0.038 to 0.093) and discharge with warfarin (OR 0.28, 95% CI 0.18 to 0.42).
Among patients managed medically the predictors of discharge without clopidogrel included discharge with warfarin (OR 0.23, 95% CI 0.15 to 0.36) and unstable angina (OR 0.59, 95% CI 0.37 to 0.92).
Conclusion: Patients with UA and undergoing CABG are systematically deprived of the benefit of dual antiplatelet therapy following hospital discharge. This treatment gap can be readily addressed.

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Intracranial hemorrhage in acute coronary syndrome: incidence, predictors, and outcomes from APPRAISE-2, PLATO, and TRACER

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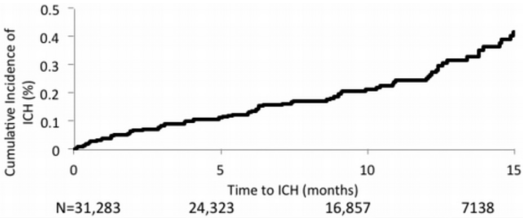
Purpose/Methods: We pooled patient-level data from cohorts with non–ST-segment elevation acute coronary syndromes (NSTE ACS) from 3 antithrombotic therapy trials to evaluate intracranial hemorrhage (ICH). Multivariable modeling identified independent predictors of ICH.
Results: Of 31,416 patients included, 108 (0.3%) had an ICH. The median follow-up was 332 (184, 434) days but differed across trials. Those with ICH were older (median 69 vs 65 years), more often had history of prior transient ischemic attack (TIA)/stroke (15% vs 8%), and had higher median baseline systolic blood pressure (SBP) (137 vs 130 mmHg). Locations of ICH were intracerebral (59%), subdural (9%), subarachnoid (9%), and intraventricular (10%). Of all ICH events, 47 (43%) were associated with death, which occurred within 30 days in 40 (85%) cases. Predictors of ICH are listed, and a Kaplan-Meier curve is displayed.

Independent predictors of ICH

	Chi square	P-value	HR (95% CI)
Prior TIA/stroke	6.80	0.009	2.07 (1.20–3.56)
Higher SBP (HR in units of 10 mm/Hg)	8.34	0.004	1.14 (1.04–1.24)
Older age (HR in units of 10 y)	8.77	0.003	1.38 (1.12–1.72)



Conclusion: In these trials, ICH was uncommon. Patients with older age, higher SBP, and prior TIA/stroke were at increased risk. ICH was associated with high mortality, and the risk increased over time. Integrating biomarker and genetic data is required to perhaps better identify ACS patients at risk of ICH.

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Clinical validation of BARC definitions of bleeding after an ACS in the TRACER trial

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Purpose: We aimed to study the relationship between Bleeding Academic Research Consortium (BARC)-graded events and mortality in the TRACER trial,