Descriptive summaries of continuous measurements are expressed as median (interquartile range [IQR]); categorical data are expressed as frequencies (%). For continuous variables, the Spearman test was used to assess for correlations, and Wilcoxon signed rank test for related samples was used to assess changes from baseline. A 2-sided p value of <0.05 was considered statistically significant. All analyses were conducted with SPSS v25.0 (IBM, New York, New York).

Overall, 36 patients agreed to participate in the study, of whom 11 (31%) required PCI. Of the patients who underwent PCI, the median age was 63 (55 to 65) years, 10 (91%) were male, and 10 (91%) white. The median model for end-stage liver disease scores was 13 (IQR: 10 to 18), and 2 (18%), 8 (73%), and 1 (9%) had Childs-Pugh Class A, B, and C cirrhosis, respectively. Baseline platelet counts were 123 (IQR: 65 to 180) 10^{12}/l, and maintenance samples were obtained 22 (IQR: 13 to 50) days from clopidogrel loading.

Median PRUs significantly decreased from baseline at all time points following clopidogrel load, with most patients responding 2 h following the dose (**Figure 1**). Percent changes from baseline were: −51% (IQR: −68% to −10%), −67% (IQR: −79% to −37%), −66% (IQR: −83% to −52%), and −59% (IQR: −86% to −27%) at 2 h, 4 h, 24 h, and maintenance point, respectively ($p < 0.01$ for paired PRU comparisons to baseline at all follow-up time points). Platelet aggregation by TEG-based mapping was similarly reduced: −73% (IQR: −100% to −33%) and -78% (IQR: −96% to −42%) at 24 h and maintenance, respectively ($p = 0.01$ for both comparisons to baseline). Impedance aggregometry yielded consistent results, with changes of −71% (IQR: −100% to −67%) and −75% (IQR: −83% to −60%) at 24 h and maintenance, respectively ($p < 0.01$ for both comparisons to baseline) (**Figure 1**).

There were no bleeding events, stent thrombosis, or acute coronary events during the period of dual-antiplatelet therapy, monitored until the maintenance point.

Limitations to this study include single-center conduct, observational design, lack of control group, and small number of patients who underwent PCI. Lastly, we excluded individuals requiring anticoagulation, limiting generalizability of these results patients receiving anticoagulants.

In conclusion, despite impaired hepatic function, patients with decompensated cirrhosis of the liver undergoing coronary angiography were found to have appropriately inhibited platelet function following clopidogrel therapy. Frequent thrombocytopenia was found at baseline, yet effects on platelet aggregation were able to be reliably monitored with the point-of-care VerifyNow P2Y12 assay and confirmed with more advanced platelet aggregation testing systems.

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RESEARCH CORRESPONDENCE

Reloading When Switching From Ticagrelor or Prasugrel to Clopidogrel Within 7 Days After STEMI

When switching from ticagrelor or prasugrel to clopidogrel early after myocardial infarction (MI), a loading dose is recommended (1,2). However, this

TABLE 1 Outcomes After Using a Loading Dose Versus No Loading Dose When Switching to Clopidogrel

	Loading Dose (n = 172)	No Loading Dose (n = 516)	p Value
Thrombotic outcome (cardiovascular death, MI, definite ST, stroke)	0 (0)	4 (0.8)	0.25
Combined bleeding outcome (PLATO major and minor bleeding)	0 (0)	3 (0.6)	0.32
PLATO major bleeding	0 (0)	1 (0.2)	0.58
PLATO minor bleeding	0 (0)	2 (0.4)	0.40

Values are n (%) of patients. Outcomes are 7 days after switch.
MI = myocardial infarction; PLATO = platelet inhibition and patient outcomes; ST = stent thrombosis.

recommendation is based solely on pharmacodynamics studies, whereas studies investigating the effects on clinical outcomes (i.e., stent thrombosis [ST] and bleeding) are lacking. In this pre-specified subanalysis of the POPular Genetics (Patient Outcome after Primary Percutaneous Coronary Intervention [PCI]) trial, we aimed to investigate the effect of loading with clopidogrel on clinical outcomes when switching from ticagrelor or prasugrel to clopidogrel early after MI.

Results of the POPular Genetics trial have been published recently (3). Noncarriers of loss-of-function alleles switching to clopidogrel within 7 days after primary PCI and with a known loading dose status were included for this analysis. The primary thrombotic outcome consisted of cardiovascular death, MI, definite ST, and stroke. The primary bleeding outcome consisted of Platelet Inhibition and Patient Outcomes (PLATO) major and minor bleeding. Both outcomes were assessed at 7 days after switching. T = 0 was defined as the moment the first dose of clopidogrel was administered. Groups were compared using Student's *t*-test, chi-square test, or 1-way analysis of variance. The log-rank test was used to calculate p values. p Values below 0.05 were considered statistically significant.

Six hundred eighty-eight patients, of whom 172 received a loading dose, were suitable for this analysis. Seventy-one received clopidogrel 300 mg, and 101 received clopidogrel 600 mg. Except for 7 patients who switched from prasugrel, the 681 other patients switched from ticagrelor to clopidogrel. Median time from primary PCI to switching was approximately 37 h (3). Most patients receiving a loading dose when switching were included after publication of the European Society of Cardiology dual-antiplatelet therapy guideline in September 2017, whereas most patients that did not were included before that date. Probably because of this, there were some clear differences in procedural characteristics. Femoral access site (34.1% vs. 15.3%), periprocedural use of glycoprotein IIb/IIIa receptor blocker (46.6% vs. 29.8%), bivalirudin use (5.9% vs. 1.2%), bare-metal stent use (5.8% vs. 0%), and multivessel disease (52.1% vs. 40.6%) were more common in the patient group not receiving a loading dose. The thrombotic outcome did not occur within 7 days of switching in patients in the loading dose group, whereas it occurred in 4 patients in the no loading dose group (0% vs. 0.8%; p = 0.25) (Table 1). Thrombotic events occurred at the day of switching (stroke and recurrent MI), at day 3 (ST) and at day 4 (coronary artery bypass surgery-related stroke). The bleeding outcome also did not occur in the loading dose group, whereas 3 patients in the no loading dose group experienced a bleeding event within 7 days after switching (0% vs. 0.6%; p = 0.32), consisting of 1 coronary artery bypass grafting surgery-related PLATO major bleeding (0.2%; p = 0.58) and 2 PLATO minor bleedings (0.4%; p = 0.19). Bleeding events occurred 3 to 5 days after switching to clopidogrel.

In conclusion, we found that very low event rates irrespective of using a loading dose, while there were numerically less thrombotic and bleeding events in the loading dose group. These results give some support for using a clopidogrel loading dose. However, due to the low event rates and lack of randomization, this study should be considered as hypothesis generating, and definitive conclusions cannot be drawn. Also, though clopidogrel may not provoke bleeding, these data cannot be extrapolated to prasugrel or ticagrelor loading doses. Furthermore, this study was performed in patients who were noncarriers of loss-of-function alleles, and results may therefore not be generalizable to carriers of loss-of-function alleles who are at increased thrombotic risk and might benefit more from a loading dose. Despite these limitations, this is the first study reporting clinical outcomes in patients using a loading dose or not. Furthermore, the decision to switch to clopidogrel was based on the trial protocol, whereas the decision to use a loading dose or not was homogenous among patients in each individual center. These decisions were therefore less susceptible to bias.

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