BACKGROUND It is unclear whether patients on oral anticoagulants (OAC) undergoing an endovascular procedure using common femoral artery (CFA) access have a higher rate of adverse events when compared to patients who are not anticoagulated with an OAC at the time of the procedure. We hypothesized that patients anticoagulated with an OAC during their index procedure have a higher rate of major adverse events including access site complications.

METHODS We retrospectively reviewed data from 779 consecutive patients who underwent a cardiac or peripheral vascular procedure at a tertiary medical center. Patients were excluded if they underwent a non CFA access. Patients were considered (group A) fully or partially anticoagulated if they had an INR≥1.6 on the day of the procedure or were on warfarin or new OAC (NOAC) within 48 hrs and 24 hrs of the procedure respectively. The non-anticoagulated group (group B) had an INR <1.6 or have stopped their warfarin and NOAC >48 hrs and > 24 hrs pre-procedure respectively. The index primary endpoint of the study was defined as the composite endpoint of major bleeding, vascular complications (AV fistula or pseudoaneurysm), or cardiovascular related death during index hospitalization. The 30-day secondary endpoint was defined as the occurrence of the index primary endpoint at index and up to 30 days post procedure.

RESULTS The index primary endpoint was met in 11/779 (1.4%) (group A: 1/27 (3.7%) versus group B: 10/752 (1.3%) (P=0.32)). The 30-day secondary endpoint was met in 18/771 (2.3%) patients. In univariate analysis, the index primary endpoint was significantly associated with female gender (P=0.024), weight <60 kg (P=0.03), prolonged procedure time (P=0.04), low hemoglobin at baseline (P=0.04), reduced creatinine clearance (CrCl) (P=0.02), and higher intra-procedural heparin dose (Units/Kg) (P=0.002) but not with anticoagulation with OAC. Logistic regression analysis for the 30-day secondary endpoint modeling for group A vs B, CrCl and weight showed that a higher CrCl (p=0.02) and lower weight (p=0.03)) but not anticoagulation with OAC (p=0.15) were independently associated with the occurrence of the 30-day composite secondary endpoint.

CONCLUSION Patients fully or partially anticoagulated with warfarin or new OAC did not have a higher 30-day composite endpoint of major bleeding, vascular complications or cardiovascular related death than those who were not anticoagulated at index procedure. Low weight and renal insufficiency were however independent predictors of these events.

CRT-300.28

Switch To Ticagrelor In Critical Limb Ischemia Anti-Platelet Study: "STT-CLIPS"

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BACKGROUND Critical Limb Ischemia (CLI) is defined as limb pain that occurs at rest, or impending limb loss caused by severe compromise of blood flow. The mortality in patients with CLI ranges from 13%-25% at 1year, mainly due to cardiovascular ischemic events. High on-treatment platelet reactivity (HPR) in patients treated with aspirin and clopidogrel is associated with increased risk of recurrent cardiovascular events after percutaneous coronary interventions. In patients with coronary artery disease, ticagrelor overcomes non-responsiveness to clopidogrel. The antiplatelet effect of ticagrelor in patients with CLI is not known. *Study Aim:* This study investigated platelet function after switching from clopidogrel to ticagrelor in patients with CLI.

METHODS Fifty patients with diagnosis of CLI (Rutherford class IV-VI) treated with clopidogrel 75 mg and aspirin 81 mg daily were tested for inhibition of platelet aggregation using the VerifyNow P2Y12 and VASP assays before and 6±1 hours after their daily clopidogrel dose. All patients were then switched from clopidogrel to ticagrelor 90 mg twice daily for 2 weeks and the VerifyNow and vasodilator-stimulated phosphoprotein (VASP) platelet reactivity assays repeated, samples were collected before and 6±1 hours after the last ticagrelor dose. For exploratory analysis, patients were divided in two groups based on the P2Y12 reaction units (PRU): Group 1. HPR on clopidogrel, defined as P2Y12 reaction units (PRU) ≥208 and Group 2. Appropriate platelet inhibition on clopidogrel (API), defined as PRU <208. *Primary Endpoint-* To determine platelet inhibition before and after switching for two weeks from clopidogrel to ticagrelor in patients with CLI. *Secondary Endpoints- 1.* Establish the proportion of patients in the HPR group who demonstrate appropriate platelet inhibition after switching to ticagrelor (PRU <208 by the VerifyNow assay) for 2 weeks. 2. Establish the proportion API group patients who demonstrate appropriate platelet inhibition after switching to ticagrelor (PRU <208 by the VerifyNow assay) for 2 weeks. *Inclusion criteria:* Patients with diagnosis of CLI (Rutherford class IV, V and VI) on continuous dual antiplatelet therapy with clopidogrel 75 mg and aspirin 81 mg daily for at least 14+2 days. *Exclusion criteria*: Chronic use of nonsteroidal anti-inflammatory drugs, thrombocytopenia (platelet count $<100 \times 10^3/\mu l$), hemoglobin <10 g/dL, use of an oral anticoagulant (warfarin) or low molecular weight heparin within 14 days, GPIIb/IIIa inhibitors, or fibrinolytic drugs within 30 days. Pregnancy, <18 or >80 years of age, current smoking (>1 pack per day), concomitant therapy with strong cytochrome P450 3A inhibitors or inducers within 14 days, concomitant antithrombotic therapy other than aspirin within 14 days, hypercoaguable states. History of medication non-compliance, drug or alcohol abuse within 2 years. Acute coronary syndrome or coronary drug-eluting stenting within 1 year. Peripheral vascular revascularization procedures (surgical or endovascular) and/or amputation within 1 month. Contraindications to ticagrelor including: hypersensitivity to ticagrelor or any of the excipients, active pathological bleeding, history of intracranial hemorrhage and severe hepatic impairment. *Data Analysis:* Data were analyzed using the SAS statistical software. The primary analysis of PRU comparisons between ticagrelor and clopidogrel before and 6 hours after daily dose was performed using a mixed-effect model with fixed effects for period, treatment, treatment sequence, and a random effect for patient within sequence. Mean on-treatment reactivity was estimated using LS means and two-sided 95% confidence intervals (CIs).

RESULTS Fifty-three patients were consented for the study and fifty completed the study. In the overall study group (n=50), mean age was 65.2±10.5 years old, 54% were male, 60% had diabetes and 24% had renal insufficiency. Vascular-related history included: 44% amputation, 38% lower extremity bypass and 86% lower extremity angioplasty. After 2 weeks of uninterrupted antiplatelet therapy, mean platelet reactivity (PRU) results were 173 PRU and 71 PRU at baseline (p<0.0001) and 140 PRU and 63 PRU after 6 hours (p<0.0001) for clopidogrel and ticagrelor, respectively. Before daily clopidogrel dose 36% (n=18) of patients demonstrated HPR and after 6 hours of clopidogrel daily dose 30% (n=15) remained with HPR. One patient (2%) had HPR on ticagrelor before and 6 hours after ticagrelor daily dose. The proportion of patients with HPR on clopidogrel who demonstrated appropriate platelet inhibition after switching to ticagrelor was 94% and all patients with API on clopidogrel remained with API after switching to ticagrelor. There were no adverse bleeding events, of the three patients who did not complete the study one was due to a skin reaction after the first ticagrelor dose and the other two patients due to events unrelated to the study (pneumonia and rheumatoid arthritis pericarditis).

CONCLUSIONS Among patients with critical limb ischemia, ticagrelor achieved significantly greater platelet inhibition than clopidogrel during the maintenance phase of treatment and 6 hours after daily dosing. High on-treatment platelet reactivity to clopidogrel in patients with CLI can be overcome by switching to ticagrelor. Additional

research is required to evaluate the potential long-term beneficial effects of enhanced platelet inhibition in patients with critical limb ischemia.

Table 1. Demographic and clinical characteristics

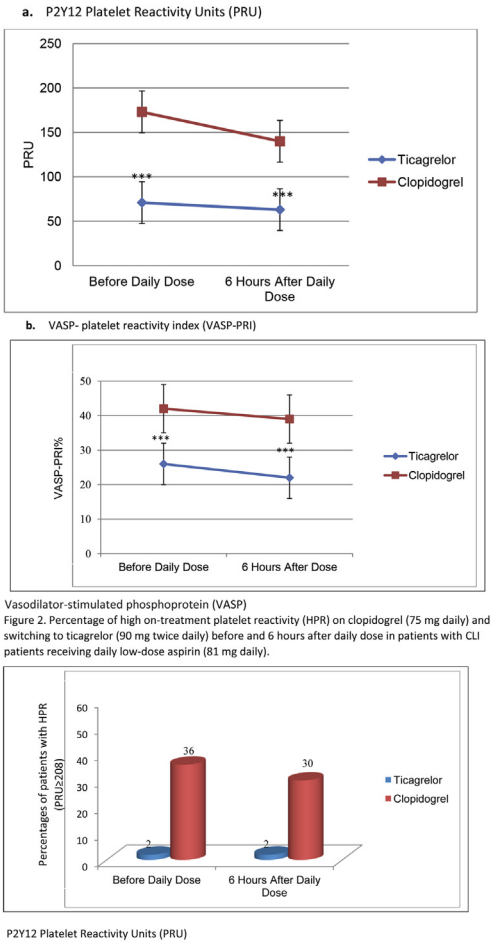
	STT-CLIPS (N=50)
Age (years), mean ± SD	65.3±10.6
Male, n (%)	27(54.0)
BMI, mean ± SD	27.7±5.1
HTN, n (%)	41(82.0)
DM, n (%)	30(60.0)
• Insulin dependent	20(40.0)
• Oral	8(16.0)
• Diet	2(4.0)
CRI, n (%)	12(24.0)
Dialysis, n (%)	4(8.0)
Dyslipidemia, n (%)	48(96.0)
History and Laboratory Data	
Current Smoker, n (%)	6(12.0)
Hemoglobin, mean ± SD	11.6±1.6
Platelet, mean ± SD	273.0±107.5
WBC, mean ± SD	8.40±2.6
Total cholesterol, mean ± SD	147.8±52.3
LDL, mean ± SD	76.7±44.4
HDL, mean ± SD	44.0±12.4
Triglyceride, mean ± SD	127.1±49.7
HbA_{1C}, mean ± SD	8.1±2.0
Albumin, mean ± SD	3.9±0.5
Vascular History	
Amputation, n (%)	22(44.0)
Bypass, n (%)	19(38.0)
Endovascular Treatment, n (%)	43(86.0)
Toe Pressures	
Before Revascularization, mmHg (mean ± SD)	28.3±23.7
After Revascularization, mmHg (mean ± SD)	84.0±44.9

Table 2. Comparative antiplatelet effect of Ticagrelor 90 mg twice daily with clopidogrel 75 mg daily before and 6 hours after daily dose in patients with CLI receiving daily low-dose aspirin (81 mg daily).

	Ticagrelor 90 mg *BID*	Clopidogrel 75 mg *QD*	LS Means Difference	P value
Before Daily Dose PRU (95% *CI*)	71 (47,94)	173(149,196)	-102 (-128, -76)	<0.0001
6 Hours After Daily Dose (95% *CI*)	63 (39,86)	140(116,163)	-77 (-110, -44)	<0.0001

CLI critical limb ischemia, *CI* confidence interval, *BID* twice daily, *QD* once daily, *PRU* P2Y12 reaction unit

Figure 1. On-treatment platelet reactivity on clopidogrel 75 mg daily and ticagrelor 90 mg twice daily before and 6 hours after daily dose in patients with CLI patients receiving daily low-dose aspirin (81 mg daily). **a.** VerifyNow P2Y12 platelet reactivity units (PRU). **b.** Vasodilator-stimulated phosphoprotein platelet reactive units (VASP-PRI).



Vasodilator-stimulated phosphoprotein (VASP)

Figure 2. Percentage of high on-treatment platelet reactivity (HPR) on clopidogrel (75 mg daily) and after switching to ticagrelor (90 mg twice daily) before and 6 hours after daily dose in patients with CLI patients receiving daily low-dose aspirin (81 mg daily).

P2Y12 Platelet Reactivity Units (PRU)

ENDOVASCULAR

CRT-300.29

Focal-Force Scoring Balloons Prior to Lutonix® 035 DCB Treatment of Femoropopliteal Denovo or Non-Stent Femoropopliteal Arterial Disease

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BACKGROUND Balloon angioplasty (PTA) remains the most commonly used primary or adjunctive device in treating femoropopliteal arteries (FP). PTA however can cause uncontrolled dissections leading to flow limitation and excessive bailout stenting. A no-stent strategy in the era of drug coated balloons is highly desirable. In this study we present data on patients pretreated with focal-force scoring balloons prior to Lutonix® DCB (Bard Peripheral Vascular).

METHODS This study is a subgroup analysis of patients pretreated with cutting /scoring balloons (cutting balloon, AngioSculpt or VascuTrak) prior to Lutonix® DCB in the SAFE-DCB prospective, multicenter US registry. This registry evaluated patient outcomes and safety following the use of the Lutonix® paclitaxel-coated angioplasty balloon (DCB) for the treatment of de-novo or restenotic lesions (non-stent) in the superficial femoral (SFA) or popliteal arteries (PA) in a real-world, heterogeneous patient population. Patients with intermittent claudication or critical limb ischemia (Rutherford 2-6) and obstructive lesions of the SFA and PA up to 150 mm in length (reference vessel diameters 4-6 mm) were enrolled. The primary effectiveness endpoint is freedom from target lesion revascularization (TLR) at 12 months, and the primary safety endpoint is a composite of