CRT-300.22

Analysis of Outcomes of In.Pact Drug Coated Balloon Use for Peripheral Vascular Disease Treatment

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INTRODUCTION Clinical studies suggested that Paclitaxel-coated balloons carry anti-proliferative properties to keep the lumen vessel open without stent requirement. We did a meta-analysis comparing the use of Medtronic In.Pact DCB to the standard uncoated balloon for the treatment of symptomatic peripheral vascular disease (PAD).

METHODS We performed a systematic search through Pub Med and Cochrane database using all RCT's that compared Medtronic In.Pact DCB to uncoated balloon for the treatment of symptomatic PAD. We stratified our analysis in femoropopliteal disease and infra-popliteal disease. Primary endpoint included symptom driven target lesion revascularization (SD-TLR) and binary re-stenosis. Secondary endpoints included death and amputations. We used fixed or random effect analysis using the Cochrane Handbook of Systematic Reviews.

RESULTS Five RCT's provided a total of 987 patients (DCB: 603 patients; PTA: 384 patients). Overall, there was a significant lower SD-TLR in the DCB compared to PTA (8.6% vs. 25%, p=0.002). Sub-analysis demonstrated significant less TLR in the femoropopliteal analysis only. There was also a trend towards less binary re-stenosis (p=0.06). Femoropopliteal group sub-analysis had significant less binary re-stenosis (p<0.001). There was no difference in amputation-free survival or mortality rates between both groups.

CONCLUSION Our analysis suggests that In.Pact DCBs are beneficial and efficacious in the treatment of symptomatic PAD, however there was no proven benefit in the reduction of amputation or mortality rates. An in-depth analysis is necessary to determine the origin of the discrepancies between the femoropopliteal and intra-popliteal analysis.

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The Effect Of Laser Energy On The Arterial Wall During The Treatment Of Femoro-popliteal Lesions: A Clirpath Excimer Laser System To Enlarge Lumen Openings (CELLO) Sub-study

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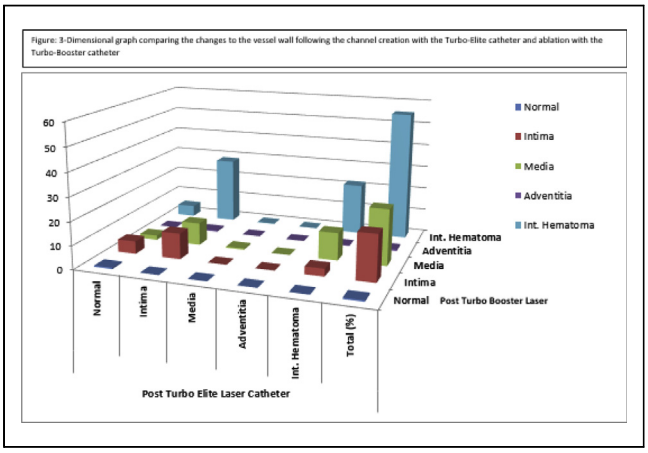
BACKGROUND The efficacy of the Excimer Laser System in the treatment of peripheral arterial diseases has been previously demonstrated in the Clirpath Excimer Laser System to Enlarge Lumen Openings (CELLO) study. The aim of this sub-study was to assess disruptions to the vessel wall following the treatment with the combination of the 2 laser catheters-Turbo-Elite and Turbo-Booster.

METHODS Intravascular ultrasound (IVUS) images from the CELLO study registry were systematically reviewed for disruptions classified as classified as intimal, medial, adventitial and intramural hematoma. The images from a total of 34 patients (1927 frames from 68 IVUS pullbacks) in the registry were successfully matched frame-to-frame to evaluate identical segments of the treated vessel in two phases; post-2mm Turbo-Elite laser pilot channel creation and post Turbo-Booster laser - direct ablation.

RESULTS The analysis revealed that the initial Turbo-Elite laser catheter successfully created a pilot channel (opening the lumen) with less than 1% media disruptions and no adventitial injury, and the combined use of the Turbo-Elite laser catheter and Turbo-Booster resulted in successful atherectomy via ablation of atherosclerotic plaques with the disruption of the vessel wall been largely limited to the media and rarely involved the adventitial layer (Figure). There were no major adverse events within the 1-year follow-up.

CONCLUSION The sub-study report supports a high safety profile for the modified excimer laser system with negligible degree of adventitial damage following ablation therapy.



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ABSTRACT WITHDRAWN

CRT-300.25

Meta-analysis of Endovascular Therapy for Renal Artery Stenosis

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INTRODUCTION Guidelines recommend endovascular therapy (EVT) for severe (>75% on angiography) renal artery stenosis (RAS). We sought to determine whether the populations studied could have influenced the lack of benefit of EVT in RAS.

METHODS Pub Med, Cochrane and EMBASE were systematically reviewed until November 2015 for all RCTs comparing EVT to medical therapy (MT) for RAS. Primary outcomes: systolic blood pressure and anti-hypertensive medication reduction. Secondary outcomes: worsening renal function, morbidity, mortality, heart failure, and stroke. We used random effect analysis according to the Cochrane-Handbook of Systematic Reviews and RevMan 5.2 for statistical analysis.

RESULTS Seven RCTs with 2126 patients were included: 1036 EVT and 1085 MT. 35-65% of patients did not have severe RAS. There was no difference in change of systolic blood pressure (0.45±1.85, p=0.64). There was a significant decrease in the mean amount of anti-hypertensive medication in the EVT group (0.24±0.12, p<0.001). There were no differences in worsening of renal function, morbidity and mortality, heart failure and stroke.

DISCUSSION Our analysis suggests that the apparent lack of added benefit of EVT for RAS could be largely secondary to selection bias, given the percentage of patients with mild to moderate RAS that were included and treated. Based on available data, trials studying EVT for severe RAS are warranted and should be designed to only include the appropriate patients. These well-designed studies are ultimately likely to "awaken the force".

CRT-300.27

Predictors of Common Femoral Artery Access Site Complications in Patients on Oral Anticoagulants and Undergoing an Endovascular Intervention

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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