Cardio Mag

Volume 1|Issue 8|2020

Dear Doctor,
*Greetings from Micro Labs Limited. We are happy to bring you "**Cardio Mag**", which contains latest and interesting news in the field of Cardiology.*

This issue contains

- ***Increased platelet inhibition after switching from prasugrel to low-dose ticagrelor in patients with prior myocardial infarction***
- ***First-in-Human Endo-Bentall Procedure for Simultaneous Treatment of the Ascending Aorta and Aortic Valve***
- ***First Cardiac Contractility Modulation Device***

Should you require any specific article or medical information, please feel free to contact us at ***medicalservices@microlabs.in***

Looking forward to your valuable feedback.
Best Regards,
Medical Team, Micro Labs Limited

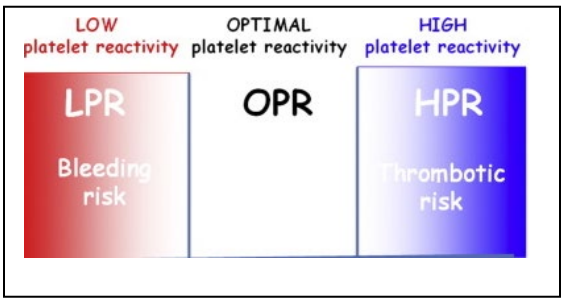
1. Increased platelet inhibition after switching from prasugrel to low-dose ticagrelor in patients with prior myocardial infarction

Antiplatelet therapy with aspirin and a P2Y12 inhibitor is standard treatment followed in patients post percutaneous coronary intervention. There is evolution of platelet P2Y12 receptor inhibitors from ticlopidine to safer clopidogrel and finally to ticagrelor and prasugrel.[1]

The aim of the current study is to assess the platelet inhibition of low dose Ticagrelor on switching over from low dose Prasugrel.

Methods:

It was a prospective, open-label study comparing platelet inhibition between low-dose ticagrelor (60 mg twice daily) and prasugrel (3.75 mg once daily)
30 patients with prior myocardial infarction (>3 months) who received aspirin and prasugrel 3.75 mg once daily were enrolled.



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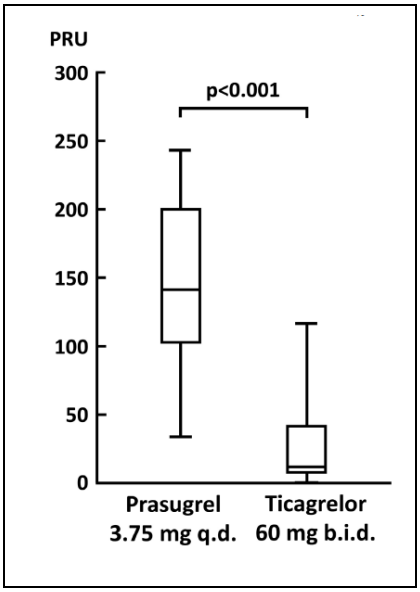
Patients were excluded if : age <20 or >85 years old, GFR <30 ml/min/1.73 m2, platelet count <10 x 104/mL, severe liver dysfunction, previous ischemic episodes or stroke , concomitant administration of oral anticoagulant or drugs that influence activity of CYP3A4, and (9) planned coronary artery bypass grafting or PCI during the study period

Prasugrel 3.75 mg was switched to ticagrelor 60 mg twice daily.

Platelet inhibition was assessed by VerifyNow assay at baseline and 14 days after switching to ticagrelor. PRU $\leq$ 95 was defined as low ontreatment platelet reactivity (LPR), PRU $\geq$262 as high on-treatment platelet reactivity (HPR), and 95 < PRU <262 as optimal treatment platelet reactivity (OPR).

Primary endpoint was comparison of PRU values between prasugrel and low-dose ticagrelor. Secondary endpoint was comparison of percentage inhibition and the prevalence of HPR, OPR, and LPR between the two groups.

Bleeding events were assessed using Bleeding Academic Research Consortium (BARC) criteria. BARC $\geq$2 was defined as major bleeding, while BARC type 1 was defined as minor bleeding.



Results:

Baseline demographic characteristics were comparable. PRU was significantly lower on ticagrelor therapy compared to prasugrel therapy [10 (7–39) vs. 143 (102–201), $p < 0.001$] as shown in figure. Ticagrelor provided higher percentage inhibition than prasugrel (88.4 $\pm$19.1 vs. 39.4 $\pm$ 21.6, $p < 0.001$). LPR was observed more frequently on ticagrelor therapy compared to prasugrel therapy (93.9% vs. 24.2%, $p < 0.001$) (Fig. 2).

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Patients treated with ticagrelor or prasugrel did not have HPR. No major adverse cardiovascular events, including stent thrombosis were seen during the study period. No major bleeding occurred during 2-week follow-up on ticagrelor therapy, while minor bleeding events were observed in 4 patients (12.1%).

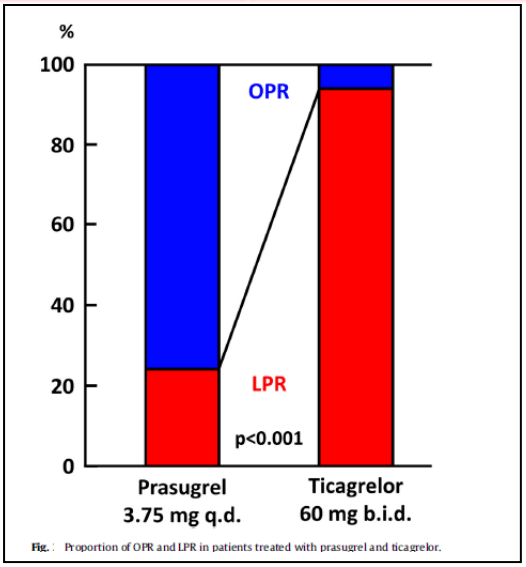

Fig. 1 Proportion of OPR and LPR in patients treated with prasugrel and ticagrelor.

Discussion:

Antiplatelet therapy is the main pharmacological treatment for secondary prevention of coronary artery disease.

Dual antiplatelet therapy (DAPT) provides more intense platelet inhibition than single antiplatelet therapy resulting in reductions in the risk of thrombotic events after percutaneous coronary intervention (PCI) or ACS.

Ticagrelor is a direct-acting, reversibly binding P2Y12 antagonist that provides rapid onset of antiplatelet effects after oral administration. It also inhibits the cellular uptake of adenosine and increases the circulating levels of adenosine, thus reducing infarct size and major adverse cardiovascular events.[3]

The current study showed that PRU on ticagrelor 60 mg twice daily was significantly lower compared to prasugrel 3.75 mg once daily and the prevalence of LPR was higher on ticagrelor therapy (no HPR was observed) as a part of DAPT.

This is the first study comparing platelet inhibition on low-dose ticagrelor therapy with that on prasugrel therapy in Japan with prior myocardial infarction.

Conclusion:

A significant platelet inhibition was seen on switching over patients from low dose Prasugrel to low dose Ticagrelor in patients with prior MI.

Reference:

1) Wander GS et al Dual antiplatelet therapy after percutaneous coronary intervention and stenting: Customize your approach. Indian Heart J Interv 2018;1:3-8.

2)Tateishi K et al. Increased platelet inhibition after switching from prasugrel to low-dose ticagrelor in Japanese patients with prior myocardial infarction. J Cardiol. 2020;75(5):473–477.

3) Degrauwe S et al. Dual antiplatelet therapy for secondary prevention of coronary artery disease. Open Heart 2017;4:e000651

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2. First-in-Human Endo-Bentall Procedure for simultaneous treatment of the Ascending Aorta and Aortic Valve

Case presentation:

A 60-year-old woman presented with repeated bleeding in neck region for 2 years. She was hemodynamically stable with no active signs of infection or heart failure. She was sedentary and in self-limitation.

On physical examination, there was a small actively bleeding cutaneous orifice in the suprasternal notch. Also she had a 2/6 systolic crescendodecrescendo murmur on auscultation.

Surgical History: patient had undergone conventional surgical aortic valve replacement in 2015. A bioprosthetic 23-mm aortic xenograft had been implanted then after a diagnosis of severe aortic stenosis.

Symptoms improvement was noted from New York Heart Association (NYHA) functional class IV before surgery to NYHA functional class I afterwards. The patient did not do regular follow up.
patient presented with visible skin bleeding arising from the suprasternal notch.

Probable differential diagnoses were true aneurysm from the aorta (or arch branches) and a pseudoaneurysm arising from the previous aortotomy.

Patient was investigated for CT angiogram that revealed a pseudoaneurysm in the suture line of the ascending aorta. Pseudoaneurysm over time had fistulized with the skin, leading to the bleeding orifice. Also showed a severely calcified porcelain aorta.

Echocardiography showed a 28-mm Hg mean gradient with reduced leaflet mobility.
Further evaluation with coronary angiogram showed no lesions in the coronary arteries, and carotid and vertebral Doppler showed no atherosclerosis.

Management:

percutaneous closure of the pseudoaneurysm was attempted initially using vascular occluders . totally , 7 devices were deployed inside the lesion without success as shown in figure .

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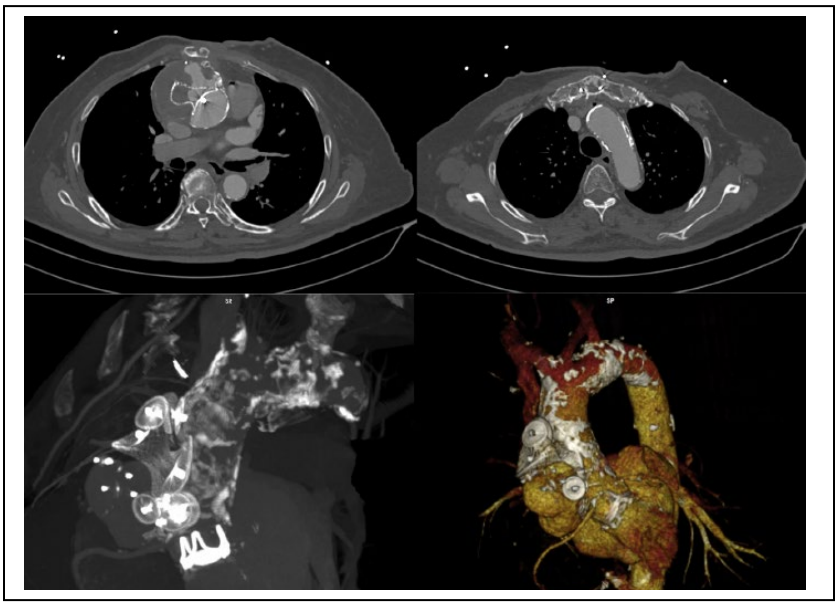
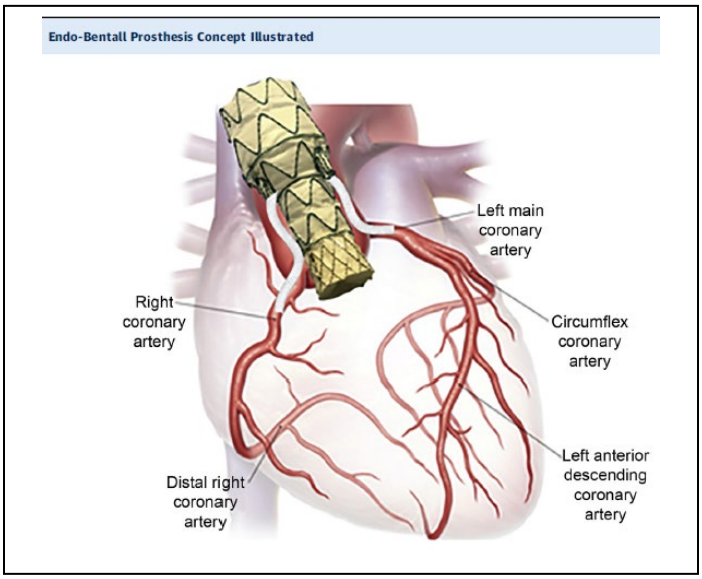


Then a completely endovascular procedure that simultaneously treating both the failing aortic valve and the pseudoaneurysm in the ascending aorta, mimicking a Bentall-De Bono procedure dubbing the Endo-Bentall procedure as shown in figure .

A custom-made device was designed as shown in figure, based on the patient's CT, including in its proximal segment a balloon-expandable transcatheter prosthesis connected to a self-expandable aortic stent.

Transcatheter valve -a modified 22-mm Braile Inovare with a chromium-cobalt frame, 20 mm in height, with 3 radiopaque markers identifying the base, valve, and skirt, and a one sheet of bovine pericardium.

Stent body with 2 branches positioned with internal and external segments, in such a way that after its release, the branches were 2 cm to the coronary ostia. In this height, the graft is reduced in diameter to the same size of the transcatheter aortic valve replacement (TAVR) (21 mm), hence providing additional space for coronary access and bridging stent deployment.



Diameter of the prosthesis at the distal ascending aorta segment was 40 mm, considering an oversize of approximately 21 % (34 mm distal aorta). Distance between the sinus tubular junction (STJ) and the

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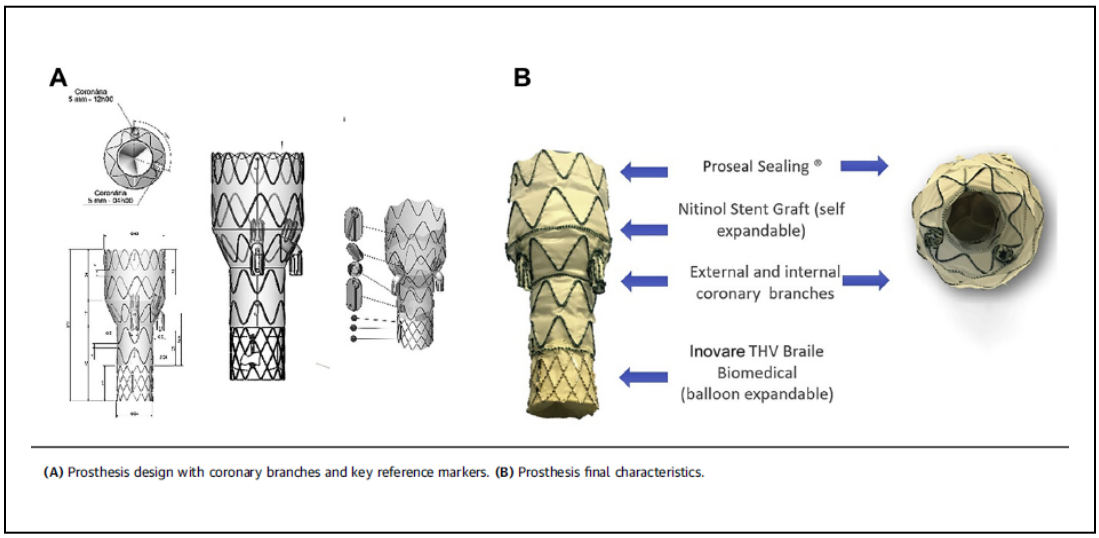
brachiocephalic trunk was approximately 6.2 cm, allowing a prosthetic segment length of 32 mm x 38 mm in diameter, used to reduce the endoleak risk.

Along with that sealing was applied to the distal prosthesis segment. Defect was a circular-shaped tear located 6 mm below the STJ, originating posteriorly near the noncoronary sinus and extending anteriorly and superiorly.

Distance from the right coronary artery to the defect was just 4 mm, making isolated aortic stenting impossible due to the absence of an adequate proximal landing zone.

Connection stents ensures coronary flow. Devices were tested in a 3-dimensional (3D) printed model of the patient's aorta, using fluoroscopy.

After pre-medication with acetylsalicylic acid 200 mg and clopidogrel 75 mg, anticoagulation with unfractionated heparin (4 mg/kg) was initiated. A temporary pacemaker was positioned in the right ventricle. Two 0.014-inch guidewires were positioned in the right and left coronary arteries. A pigtail was also positioned in the aortic root with the aid of a guidewire.
Left ventricular apex was punctured with a 6-F introducer. A stiff guidewire was used to cross the failed



(A) Prosthesis design with coronary branches and key reference markers. **(B)** Prosthesis final characteristics.

bioprosthetic aortic valve, and the introducer was exchanged for a 30-F introducer. Rapid pacing was used to achieve controlled hypotension. Main body of the stent was slowly deployed in the ascending aorta and later, the balloon was expanded to inflate the transcatheter heart valve
Then restored the Pressure . Both transesophageal echocardiography and angiography showed effective release .The ventricular apex was closed. Extracorporeal membrane oxygenation (ECMO) support was initiated prior to any attempts at coronary cannulation.

Right coronary artery was cannulated first through the inside of the main stent body by using a 5 x 58 mm stent . In the left coronary artery, the stent positioning was not successful. The operator switched

to a 8x 56 mm stent which worked adequately.

After procedure angiogram showed no leaks and patent ostia. Control echocardiography showed normal valve function with a low mean gradient of 9 mm Hg.
procedure time was 6 hours. After procedure CT showed no endoleak and patent coronary connecting stents.

Discussion:

Usual management of the case is Bentall-De Bono procedure, replacing the ascending aorta and the failed aortic bioprosthesis, however this patient denied surgery, hence new technique was planned carefully that provided therapeutic opportunity for patients with inoperable conditions .
However in this procedure long term patency is questionable and also TAVR durability is a concern considering patient age. As an alternative in this patient, use of multiple TAVR in- TAVR procedures should have been used.

In this case, supra-annular device should be considered in this scenario in order to provide a lower post-operative gradient if a TAVR in- TAVR procedure is needed.
There was no evidence of instability during the procedure, but ECMO was used for a short time to ensure there would be no complications .

Conclusion:

Endo Bentall procedure is a suitable procedure for combined valvular and ascending aortic disease in inoperable conditions.

Reference:

Gaia DF et al. First-in-Human Endo-Bentall Procedure for Simultaneous Treatment of the Ascending Aorta and Aortic Valve. JACC: Case Reports. 2020 ; 2 (3) : 480-5.

3. First Cardiac Contractility Modulation Device

A new device has been designed to improve myocardial contractility in patients with heart failure. The system is been intended to improve quality of life of heart failure patients by reducing the severity of their symptoms.

Presently many heart failure patients have few options in terms of effective treatments to reduce and control their symptoms. Medication help certain patients, but some still experience unacceptable symptoms.

Pacemakers are beneficial for some, but not all patients, and they do not increase the effect of cardiac output.

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The Optimizer is an implantable device that delivers electrical impulses to the heart specifically to improve myocardial contractility, using a technique known as Cardiac Contractility Modulation (CCM). The device connects to the heart through two leads that deliver electrical impulses at a specific time during the heart cycle, increasing the systolic contraction of the myocardium. Increasing cardiac contraction improves quality of life for heart failure patients and thereby their ability to perform daily activities, such as walking.

Approved by the FDA in 2019, the device is under study to substantiate safety and efficacy in heart failure patients

Reference:
Avaialble at:
https://www.medgadget.com/2020/04/optimizer-system-for-cardiac-contractility-modulation-interview-with-dr-ishu-rao-medical-director-of-impulse-dynamics.html. Accessed on 016-04-2020.

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