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Review

Review of Late-Breaking Trials From CRT 2021 Virtual

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Abbreviations: BASILICA, Bioprosthetic Aortic Scallop Intentional Laceration to prevent Iatrogenic Coronary Artery obstruction; BCrI, Bayesian credible interval; BP-SES, biodegradable-polymer sirolimus-eluting stents; BVS, bioresorbable vascular scaffold; CI, confidence interval; CRP, C-reactive protein; CT, computed tomography; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; DOAC, direct oral anticoagulants; DP-EES, durable-polymer everolimus-eluting stent; hs, high sensitivity; IVUS, intravascular ultrasound; MACE, major adverse cardiovascular event; MI, myocardial infarction; NC, non-compliant; NHLBI, National Heart, Lung and Blood Institute; NIH, National Institutes of Health; NRP, no-reflow phenomenon; NSTEMI, non-ST-elevation myocardial infarction; NYHA, New York Heart Association; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; PF-AES, polymer-free amphilimus-eluting stents; POBA, plain old balloon angioplasty; PP-ZES, permanent-polymer zotarolimus-eluting stent; QCA, quantitative coronary arteriography; STEMI, ST-segment elevation myocardial infarction; STJ, sinotubular junction; STR, ST-segment resolution; TAVR, transcatheter aortic valve replacement; TIMI, Thrombolysis in Myocardial Infarction; TLF, target lesion failure; TLR, target lesion revascularization; TV-MI, target vessel-related myocardial infarction; VARC-2, Valve Academic Research Consortium-2; VTC, valve-to-coronary.

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1. Introduction

Since March 2020, the coronavirus disease 2019 (COVID-19) pandemic has redefined the way in which cardiology conferences have been held. Cardiovascular Research Technologies (CRT) 2020 was the last in-person cardiology meeting in 2020 just before the outbreak of COVID-19 in the U.S. Nearly a year later, given the continued presence of COVID-19, CRT 2021 transitioned into a fully virtual meeting. In this article, we present a brief overview of late-breaking clinical trials presented at CRT 2021 Virtual.

2. Structural

2.1. Clinical outcomes after BASILICA and TAVR in 214 patients

Presenter: Dr. Jaffar Mohammad Khan

Key Points: The novel leaflet laceration procedure known as Bioprosthetic Aortic Scallop Intentional Laceration to prevent Iatrogenic Coronary Artery obstruction (BASILICA) was shown to be safe and feasible in a real-world setting for the prevention of iatrogenic coronary artery obstruction during transcatheter aortic valve replacement (TAVR) in the largest registry study to date.

The results were reported by Jaffar M. Khan, BM, BCh, PhD, of the National Heart, Lung and Blood Institute (NHLBI) at the National Institutes of Health (NIH), Bethesda, Maryland, and MedStar Washington Hospital Center, Washington, DC [1]. Khan and colleagues' findings were simultaneously published in *JACC: Cardiovascular Interventions* [2]. Khan was co-inventor of the catheter devices used to lacerate aortic valve leaflets in the BASILICA procedure, which was in turn developed by the NIH. While rare – occurring in just 0.7% of TAVR cases – coronary artery obstruction is a "devastating" complication with suboptimal preventative strategies, Khan and colleagues noted in 2019 when results from the prospective multicenter BASILICA trial (enrolled in 2018) were first reported [3].

Coronary obstruction has a 40% to 50% mortality rate, Khan said, as he reported new findings from a larger cohort of 214 patients. These patients were enrolled between June 2017 and December 2020 across sites in North America and Europe. The retrospective, multicenter, single-arm registry study was aimed at determining the safety of the procedure and its feasibility in a real-world setting – data that were previously lacking. The new study included patients who had received BASILICA to prevent coronary artery obstruction but excluded patients from the existing BASILICA trial.

Patients in the registry had a mean age of 74.9 $\pm$ 10.6 years, 68.7% were women, and the majority (54%) were considered high-risk. Aortic stenosis (AS) was present for 85.9% and aortic regurgitation (AR) in 14.1%. During TAVR procedures, 60.1% received a SAPIEN 3 (Edwards Lifesciences, Irvine, California) and 39.9% received a CoreValve Evolut R or PRO (Medtronic, Minneapolis, Minnesota), while the majority of access was transfemoral (91.1%). The majority of patients (72.8%) had previous bioprosthetic aortic valves, and 78.5% underwent single-leaflet BASILICA. Procedural success overall – defined as successful BASILICA traversal and laceration without mortality, coronary obstruction, or emergency intervention – was achieved in 86.9% of patients. Successful leaflet traversal was reported in 94.9%, successful leaflet laceration in 94.4%, no culprit coronary obstruction found for 95.3% of cases, and no emergency surgery or re-intervention for 93%. There was a 100% procedural survival rate.

Valve Academic Research Consortium-2 (VARC-2) definitions were used to adjudicate events. At 30 days, 5.7% of patients had coronary obstruction, including non-culprit obstructions, while just 2.8% died. Stroke occurred in 2.8% (0.5% of which were disabling), 3.3% had a life-threatening bleed, 3.8% had a major vascular complication, and 4.3% had acute kidney injury. Outcomes were similar between single- and double-leaflet BASILICA, native and bioprosthetic valve, and with use of cerebral embolic protection. VARC-2 safety at 30 days was marked for 82.8%. Khan reported secondary endpoint results including a 3.3% rate of periprocedural myocardial infarction (MI), 0.5% pericardial effusion or cardiac tamponade, 8.5% procedural hypotension requiring pressors, and 1.4% endocarditis. At 1 year, 124 patients (83.9%) were alive.

The study demonstrated that BASILICA is safe, with low rates of stroke and death, said Khan. He added that more importantly, the study demonstrates the BASILICA procedure to be safe in a real-world setting in centers with appropriate training, leading to high rates of success and low rates of coronary artery obstruction.

"This reassuring data should facilitate wider dissemination of the BASILICA procedure at high-volume centers," Khan concluded.

2.2. Off-label use of direct oral anticoagulants in patients receiving mechanical and bioprosthetic heart valves: Insights from the Society of Thoracic Surgeons National Database

Presenter: Dr. Ankur Kalra

Key Points: Off-label use of direct oral anticoagulants (DOACs) has recently risen among patients with bioprosthetic heart valves in the US, despite their use being off-label.

This is according to an analysis of the Society of Thoracic Surgeons Adult Cardiac Surgery Database (version 2.81), which included data from patients undergoing surgical aortic or mitral valve replacement with either mechanical or bioprosthetic heart valves between July 2014 and June 2017. The results were reported by Ankur Kalra, MD, of the Cleveland Clinic [4].

The trend for DOAC use among patients with mechanical heart valves was also present despite being contraindicated across medical literature. Use of DOACs in patients with mechanical valves is specifically contraindicated, Kalra said, while DOAC use in patients with bioprosthetic valves is off-label. There are no randomized data reporting the safety of DOACs in bioprosthetic valves, he said, adding that the RE-ALIGN (Randomized, Phase II Study to Evaluate the Safety and Pharmacokinetics of Oral Dabigatran Etexilate in Patients after Heart Valve Replacement) trial reported harm with dabigatran use in mechanical valves. Kalra also listed examples of prescribing information for some commonly used DOACs, including rivaroxaban and apixaban – both of which are not recommended for use with prosthetic heart valves – and dabigatran, which lists mechanical heart valve as a contraindication. Still, despite the warnings, DOAC use has continued for some heart-valve patients and, according to the registry, grew during the study period for those with bioprosthetic heart valves. The trend of DOAC use among patients with mechanical heart valves remained similar throughout.

Kalra reported that DOAC use at discharge was seen overall for 1.1% (193 of 18,142) of aortic-mechanical-valve patients, 1.04% (139 of 13,942) of mitral-mechanical-valve patients, 5.89% (2180 of 39,243) mitral-bioprosthetic-valve patients and 4.66% (5625 of 116,203) of aortic-bioprosthetic-valve patients. Drawing comparisons to warfarin use in patients with mechanical heart valves, those who received DOACs were older (mean age 60.8 years vs. 53.0 years) and had a higher prevalence of comorbidities – including hypertension (83% vs. 68%), arrhythmia (47% vs. 30%) and peripheral arterial disease (18% vs. 7%). They were more likely to have been on a DOAC preoperatively compared to the mechanical-heart-valve patients who received warfarin. Patients with bioprosthetic heart valves who received DOACs were also older (mean age 66.3 years vs. 65.0 years), had a higher prevalence of co-morbidities – particularly arrhythmia (90% vs. 42%) – and had a higher percentage of DOAC use preoperatively than those given warfarin. Prosthetic valve patients receiving DOAC had higher postoperative (before discharge) incidence rates, such as pulmonary embolism – 1.1% for mechanical valve patients given DOAC vs. 0.04% for those given warfarin, and 0.37% for DOAC bioprosthetic valve patients vs. 0.30% on warfarin – and deep vein thrombosis – 3.0% vs. 0.4% in the

mechanical group, and 2.1% vs. 1.5% for bioprosthetic – compared with prosthetic valve patients receiving warfarin, he said.

Although the study lacks follow-up data to fully compare outcomes of DOACs vs. warfarin in prosthetic-heart-valve patients, Kalra said the study suggests prevailing off-label use of DOACs in patients with prosthetic heart valves, "despite satisfactory safety data."

"Until the completion of randomized clinical trials that provide sufficient evidence for DOAC use, physicians may wish to exercise caution with regard to DOAC prescription in patients with prosthetic valves," he concluded.

2.3. Coronary obstruction from TAVR in native aortic stenosis: Anatomic predictors from two large global registries

Presenter: Dr. Jaffar Mohammad Khan

Key Points: Patients undergoing TAVR with a cusp height equal to or greater than their coronary height could be at greater risk of coronary obstruction, as could those with a valve-to-coronary (VTC) distance of less than 4 mm and calcium volume greater than 600 mm^3.

The findings from a retrospective, multicenter, single-arm study of the Coronary Obstruction with TAVR (CO-TAVR) and Coronary Obstruction Risk Assessment (COBRA) registries – supported in part by TAVR device manufacturer Medtronic – were presented by Jaffar M. Khan, BM, BCh, PhD, of the NHLBI and MedStar Washington Hospital Center [5]. Khan disclosed that he is proctor for both Medtronic and Edwards Lifesciences.

Screening for coronary obstruction today is unidimensional, Khan noted, adding that it is based on the 2013 findings of just 27 computed tomography (CT) scans – a study that concluded coronary artery obstruction from TAVR occurs more frequently in women, in those receiving balloon-expandable valves, and in those with a previous surgical bioprosthesis. The present study, therefore, set out to determine risk factors by analysis of the CT anatomical features of patients with native AS who developed coronary obstruction in a larger patient cohort using advanced multidimensional measurements based on obstruction pathology.

The researchers included 60 patients from the CO-TAVR and COBRA registries who had coronary obstruction after TAVR between January 2011 and December 2020 across 22 centers in Asia, North America, South America, and Europe, excluding embolic obstruction. A cohort of 1381 patients with CT and no coronary obstruction between May 2013 and October 2020 were included from the MedStar aortic-valve-stenosis database as controls. The data confirmed coronary obstruction as a risk factor overall, with 26.7% of patients with coronary obstruction dying in the hospital compared to 0.7% of those in the non-obstruction group. Of the 60 coronary-obstruction patients, 58.3% were women vs. 47.1% in the no-obstruction group. Age ranges between the two cohorts were similar (mean age 79.6 years vs. 79.3 years). For those with coronary obstruction, 46.6% received a balloon-expandable valve, 46.6% a self-expanding valve, and 6.8% a mechanically expandable valve. The same data were yet to be ascertained for those without obstruction. Coronary obstruction occurred more often in the left coronary system (47 patients, 78.3%) compared to the right coronary system (10 patients, 16.7%) or both (3 patients, 5%). Aortic annular area was smaller in the obstruction group than in those without obstruction (415 ± 89 mm^2 vs. 468 ± 103 mm^2; $p < 0.001$), as was annular perimeter (70.6 ± 13.7 mm vs. 77 ± 8.1 mm; $p < 0.002$). For those with coronary obstruction, coronary height was 10.8 ± 3.3 mm on the left and 12.2 ± 1.7 mm on the right vs. 13.1 ± 3 mm and 15.5 ± 3.4 mm, respectively, for the no-obstruction group. Sinus diameter was smaller, at 29.8 ± 3.4 mm on the left and 26.3 ± 2.6 mm on the right for obstruction patients vs. 32.7 ± 4.1 mm and 31.1 ± 4 mm for the no-obstruction patients, respectively. Sinotubular junction (STJ) height and diameter were also smaller in patients with obstruction compared with controls (STJ height left 17.5 ± 2.9 mm and right 17.8 ± 2.5 mm for the obstruction groups vs. STJ height left 21.9 ± 4.2 mm and right 22.4 ± 4.2 mm for the non-obstruction group; STJ diameter 26.2 ± 3.1 mm vs. 29.6 ± 3.7 mm, respectively).

"However, these dimensions alone are poor discriminators for coronary obstruction," Khan noted. He stressed that cusp height greater than or equal to coronary height appears to be an important mechanism for obstruction, with 96.6% sensitivity. A VTC of less than 4 mm or calcium volume over 600 mm^3 also had 95.6% sensitivity for coronary obstruction, he concluded.

2.4. TAVR in low-risk patients with bicuspid aortic stenosis: 1-year results from the LRT trial

Presenter: Dr. Toby Rogers

Key Points: Clinical outcomes for low-risk bicuspid AS patients who underwent TAVR in the Low Risk TAVR (LRT) trial remained "excellent" at 1 year.

TAVR is approved for low-risk tricuspid patients in the US; however, data on TAVR in low-risk patients with severe bicuspid AS are lacking. The bicuspid registry of the LRT trial sought to elucidate the safety and efficacy of TAVR in these patients. The results were presented by investigator Toby Rogers, MD, PhD, of MedStar Washington Hospital Center and the NHLBI [6]. Bicuspid patients were excluded from the LRT trial, but the trial's bicuspid registry enrolled 72 patients between 2016 and 2020. Patients had a mean age of 68.1 ± 7.7 years, were majority women (54.2%), and 15 (20.8%) had a New York Heart Association (NYHA) functional class III or IV. Initial results from the bicuspid registry of the LRT trial were presented in February 2020, demonstrating that TAVR was safe and effective for low-risk bicuspid patients, hitting the zero-mortality goal, while also achieving zero disabling strokes. At 1 year, only one patient died, a sudden death 291 days after TAVR with no post-mortem performed. Three patients had suffered non-disabling strokes (4.5%), and two had new-onset atrial fibrillation (3%). Nine patients received a new permanent pacemaker implantation within the year.

Rogers drew comparisons with tricuspid patients, noting that those with bicuspid AS tended to be younger but that the subclinical leaflet thrombosis rate was found to be similar between the two groups. Finally, only a minority of patients in the bicuspid analysis had Sievers Type 0 morphology (no raphe), he added; thus, the results of this trial could not be applied to patients with Sievers Type 0 anatomy.

3. Coronary

3.1. Randomized comparison of biodegradable-polymer sirolimus-eluting stents versus durable-polymer everolimus-eluting stents in patients with ST-segment elevation myocardial infarction: Final 2-year outcomes of the BIOSTEMI randomized trial

Presenter: Dr. Thomas Pilgrim

Key Points: Biodegradable-polymer drug-eluting stents (DES) may further improve clinical outcomes versus durable-polymer DES in patients with acute ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous coronary intervention (PCI), researchers concluded from the final 2-year outcomes of the Biodegradable Polymer Sirolimus-Eluting Stent With a Durable Polymer Everolimus-Eluting Stent for Patients With Acute ST-Segment Elevation Myocardial Infarction (BIOSTEMI) trial.

The latest BIOSTEMI results were presented by one of the study's lead researchers, Thomas Pilgrim, MD, MSc, of Bern University Hospital, Switzerland, and simultaneously published online in *JACC: Cardiovascular Interventions* [7,8]. DES is the standard for mitigating repeat revascularizations in PCI compared with bare-metal stents. The newest generation of DES have reduced strut thickness of the metallic stent platform and use biodegradable polymers as a carrier for the antiproliferative substance. BIOSTEMI, therefore, aimed to compare safety and efficacy of the newest-generation biodegradable-polymer

sirolimus-eluting stents (BP-SES) with older durable-polymer everolimus-eluting stent (DP-EES) technology using Bayesian methods in 1300 STEMI patients with 1623 lesions, randomly allocated one of the treatment options between April 2016 and March 2018.

Consistent with 1-year follow-up, BIOSTEMI data at 2 years demonstrated that patients given BP-SES had superior outcomes in terms of target-lesion failure (TLF), a composite of cardiac death, target-vessel myocardial re-infarction, and clinically indicated target-lesion revascularization (TLR). Follow-up at 2 years was completed for 94% (1221) of patients. At 2 years, TLF occurred in 33 patients (5.1%) treated with BP-SES and in 53 patients (8.1%) treated with DP-EES (rate ratio: 0.58; 95% Bayesian credible interval [BCrI]: 0.40 to 0.84; Bayesian posterior probability of superiority = 0.998). The difference was still "robust" after the exclusion of historical information from the BIOSCIENCE trial (rate ratio: 0.62; 95% BCrI: 0.40 to 0.96; Bayesian posterior probability of superiority = 0.985). The result was driven by lower rates of ischemia-driven TLR, the researchers added. Clinically indicated TLR in patients treated with BP-SES occurred in 2.5% compared with 5.1% for DP-EES (rate ratio: 0.52; 95% BCrI: 0.30 to 0.87; Bayesian posterior probability of superiority = 0.993). There were no significant differences in rates of cardiac death (2.9% for BP-SES vs. 3.2% for DP-EES; rate ratio: 0.77; 95% BCrI: 0.44 to 1.35; Bayesian posterior probability of superiority = 0.823), target-vessel myocardial re-infarction (1.5% vs. 2%; rate ratio: 0.67; 95% BCrI: 0.33 to 1.34; Bayesian posterior probability of superiority = 0.875), and definite stent thrombosis between the two treatment arms (1.4% vs. 1.8%; rate ratio: 0.73; 95% BCrI: 0.30 to 1.69; Bayesian posterior probability of superiority = 0.771). There were no differences in patient-oriented clinical outcomes and stent thrombosis.

"The use of biodegradable-polymer DES may further improve clinical outcomes in patients with acute STEMI undergoing primary PCI," the researchers concluded.

However, with no difference observed between these treatment groups in the preceding BIOSCIENCE randomized trial, Royal College of Surgeons in Ireland, Dublin, colleagues Robert A. Byrne, MB, BCh, PhD – also of Mater Private Hospital, Dublin, – and J.J. Coughlan, MB, BCh – also of Technische Universität München, Munich – exercised caution in their accompanying editorial [9].

"These data are encouraging but should be interpreted in the context of previous large scale trials comparing the biodegradable-polymer sirolimus-eluting stent with other frequently used contemporary DES," they noted. "Expressed in Bayesian terms, it remains to be seen whether the present data are sufficient to update our a priori beliefs."

The BIOSTEMI trial received a dedicated research grant from the maker of the experimental stent – the Orsiro BP-SES (Biotronik). The researchers also list relationships with the maker of the control device, the Xience DP-EES (Abbott), and with other device manufacturers, including Edwards Lifesciences and Boston Scientific.

3.2. 3-year results from the COMPARE-ABSORB trial

Presenter: Dr. Pieter C. Smits

Key Points: Three-year COMPARE-ABSORB trial results show no significant difference in outcomes between the newer-generation Absorb bioresorbable vascular scaffold (BVS) and the Xience DES for patients at high risk of restenosis following PCI.

A specific BVS implantation technique has never been employed from the start in previous randomized clinical trials for the Absorb device. COMPARE-ABSORB – a trial with grant funding from Abbott, the manufacturer of both devices in the trial – was therefore launched with a dedicated optimal implantation technique for BVS, which includes mandatory pre-dilation with 1:1 balloon-artery ratio and high pressure (>16 atm) post-dilation. The findings from the COMPARE-ABSORB trial were presented by principal investigator Pieter C. Smits, MD, of Maasstad Hospital Rotterdam, Netherlands [10]. Treatment of target vessels less than 2.75 mm measured by quantitative coronary arteriography (QCA), intravascular ultrasound (IVUS), or optical coherence tomography (OCT), and post-dilation with non-compliant (NC) balloons up to 0.5 mm larger than the scaffold are also recommended. The hypothesis was that, after full resorption, the BVS procedure could lead to better long-term outcomes for a high-risk population for restenosis compared to PCI with the metallic DES.

In order to find the patient population that could potentially benefit most from the vascular restoration therapy concept in the long term, the patient selection included those with complex lesions not investigated in previous randomized studies. Those with STEMI, acute non-ST-elevation myocardial infarction (NSTEMI), bifurcations, long lesions, and chronic total occlusions, and patients at high risk for restenosis due to known diabetes and/or multivessel disease, of which more than one *de novo* target lesion were to be treated with the study scaffold/stent, were included. The trial also included those with complex *de novo* target lesions, characterized as lesion length of more than 28 mm, small vessels (reference vessel diameter between 2.25 and 2.75 mm), lesions with pre-existing total occlusion, or bifurcation with a single device strategy.

The trial's original planned enrollment was 2100 patients. However, after results of earlier studies showed increased rates of major adverse events, specifically, MI and scaffold thrombosis, in patients receiving the Absorb stent when compared to patients treated with the Xience stent, Abbott recalled the Absorb stent and then pulled it from the market in 2017. The COMPARE-ABSORB study stopped enrolling patients shortly before the stent was no longer available for sale. At that point, 1670 patients were enrolled. According to ClinicalTrials.Gov, those patients were enrolled across 44 study sites in Europe (848 randomized to Absorb with 1242 target lesions and 962 procedures vs. 822 to Xience, with 1213 target lesions and 904 procedures) [11].

Patient characteristics were similar across the two groups, with a mean age of 61.9 ± 9.4 years for Absorb vs. 62.2 ± 9.0 years for Xience, and respectively, 79.5% vs 76.3% male patients, 34.6% vs. 36.1% diabetic, 28.8% vs. 26.9% currently smoking, and 71.6% vs. 69.2% with hypertension. The Absorb group was composed of 13% STEMI patients vs. 12.5% for Xience, and respectively, 13.3% had received treatment for NSTEMI within 72 h vs. 12.4%. At 1 year, there was no assumed difference between the Xience and Absorb devices and a 4.5% non-inferiority margin. TLF – a device-oriented composite endpoint of cardiac death, target-vessel MI, and clinically-indicated TLR – was seen for 4.2% of those given Xience vs. 5.1% given Absorb. By 3-year follow-up, TLF rates were still not significantly different between the ABSORB and Xience groups (8.9% vs. 7.4%; hazard ratio: 1.21; 95% confidence interval [CI]: 0.86 to 1.70; $p = 0.27$).

"Whether the absence of increased risk (of) very-late scaffold thrombosis and TV-MI (target vessel-related myocardial infarction) was prevented by a dedicated implantation technique or prolonged dual antiplatelet therapy (DAPT) remains to be determined," Smits said. "Follow-up of 7–10 years within COMPARE-ABSORB will show whether Absorb has long-term advantages above the metallic Xience stent."

3.3. Three-year clinical outcomes after implantation of a permanent-polymer zotarolimus-eluting stent versus a polymer-free amphilimus-eluting stent: Landmark analysis of the Recre8 trial

Presenter: Dr. Michiel Voskuil

Key Points: Polymer-free amphilimus-eluting stents (PF-AES) were clinically noninferior to permanent-polymer zotarolimus-eluting stents (PP-ZES) in terms of TLF 3 years after PCI in the ReCre8 trial.

The results were reported by Michiel Voskuil, MD, PhD, of the University Medical Center Utrecht, Netherlands [12]. The researchers said PF-AES possess multiple properties that improve targeted drug elution without the presence of a permanent polymer. However, their clinical performance has not yet been compared to the latest-generation permanent-polymer DES in a large randomized study, introducing

shortened DAPT in troponin-negative patients alongside a "considerable population" of troponin-positive patients with prolonged follow-up.

The ReCre8 trial's aim was, therefore, to study noninferiority between the two types of new-generation devices with TLF as an endpoint in an "all-comer" population through 3-year post-implantation follow-up. TLF was defined as a composite of cardiac death, target-vessel MI, and TLR. Between November 2014 and July 2017, a total of 1491 patients were randomized to either a PP-ZES (Resolute Integrity, Medtronic) or PF-AES (Cre8, Alvimedica). PF-AES was found to be clinically noninferior to PP-ZES between 1 and 3 years. During this period, the primary endpoint of TLF occurred in 35 patients (4.9%) in the PP-ZES arm vs. 37 (5.1%) in the PF-AES arm (hazard ratio: 1.04; 95% CI: 0.66 to 1.66; p-interaction = 0.80). Clinical noninferiority of the PF-AES device was confirmed with a risk difference of 0.2% (upper limit 1-sided 95% CI 2.2%; p-non-inferiority = 0.0031). DAPT duration was similar in both arms, with 12 months in troponin-positive patients and 1 month in troponin-negative patients. Cardiac death occurred in 11 (1.5%) of PP-ZES patients vs. 14 (1.9%) of PF-AES patients (p-difference = 0.57), and respectively, target-vessel MI occurred in six (0.8%) versus eight (1.1%) patients (p-difference = 0.61), while TLR happened in 23 (3.2%) vs. 22 (3.1%) (p-difference = 0.84). One case of stent thrombosis occurred in the PP-ZES arm (0.1%), while no cases were seen in PF-AES patients.

The results show that PF-AES is clinically non-inferior to PP-ZES at long-term follow-up, said Voskuil, adding that "no late catch-up phenomenon (was) visible."

3.4. Pre-procedural colchicine in patients with acute ST-elevation myocardial infarction undergoing percutaneous coronary intervention: A randomized controlled trial (PodCAST-PCI)

Presenter: Dr. Yaser Jenab

Key Points: Colchicine did not significantly reduce the rate of no-reflow phenomenon (NRP) or improve cardiovascular outcomes when administered immediately before primary PCI in patients with STEMI according to follow-up over 1 year in the PodCAST-PCI trial.

The late-breaking results were presented by Yaser Jenab, MD, of Tehran University of Medical Sciences, Iran [13]. The primary mechanism of action of colchicine is tubulin disruption, leading to inhibition of microtubule polymerization, he said – "an essential component of cellular cytoskeleton." In turn, this promotes potential anti-inflammatory effects, "especially mediated by its capability to concentrate and act on granulocytes," according to Dr. Jenab. Studies have suggested that administering the medicine at 0.5-mg dosages to those with stable coronary disease and those with recent MI can lower risk of further cardiovascular events. PodCAST-PCI was, therefore, launched to evaluate the role of pre-procedural administration of colchicine on reducing NRP and improving cardiovascular outcomes in patients with acute STEMI undergoing primary PCI.

The single-center randomized double-blind trial – conducted at Tehran Heart Center – included 321 patients given either a 1-mg colchicine tablet just after assignment for PCI and 0.5 mg after the procedure (161 patients), or a matching placebo formulation (160 patients). All patients were also treated with routine medications for acute MI, including 300 mg of aspirin, 600 mg of clopidogrel, and 80 mg of atorvastatin. The NRP primary endpoint was defined as Thrombolysis in Myocardial Infarction (TIMI) flow grade of less than 3 after PCI, or – if the TIMI flow grade was 3 – TIMI flow grade after PCI of zero or 1. Secondary endpoints included major adverse cardiovascular events (MACE) at 1 month and 1 year, ST-segment resolution (STR), high sensitivity (hs) troponin T at baseline, 24 h, and 48 h after PCI, P-selectin at baseline and 24 h, and high-sensitivity C-reactive protein (hs-CRP) at baseline and 48 h.

Baseline characteristics were similar between the two groups, with male patients comprising 78.9% of the colchicine group vs. 79.4% of the control group and, respectively, a mean age of 58.74 ± 10.39 years vs. 58.98 ± 11.20 years, 32.9% of colchicine patients with diabetes mellitus vs. 38.1% of control patients, and 40.4% of the colchicine group with hypertension vs. 38.8% of the control group. Pain-to-device time was 235 min for the colchicine group vs. 265 min for the control. The mean stent lesion length was 12.75 mm for the treatment group and 13.15 mm for placebo, and respectively, 15 (9.3%) vs. 13 (8.1%) had plain old balloon angioplasty (POBA), 50 (31.1%) vs. 43 (26.9%) had direct stenting, 111 (69.4%) vs. 113 (70.6%) had pre-dilation ballooning, while 90 (55.9%) vs. 82 (51.2%) had post-dilation ballooning. In each group, 23 patients (14.4%) had no-reflow, and two patients from each group died. In the treatment group, 30 (18.6%) had STR below 50% compared to 37 (23.1%) in the control group, 27 (16.8%) in the treatment group had STR between 50% and 70% compared to 25 (15.6%) in control, while 104 (64.6%) colchicine-treated patients had STR above 70%, compared to 98 (61.3%) in the control group ($p = 0.32$). MACE at 1 month occurred in seven (4.3%) patients on colchicine compared to 12 (7.5%) on placebo ($p = 0.23$), and occurred in 15 (9.3%) and 18 (11.2%) at 1 year, respectively ($p = 0.54$). By 48 h, mean troponin was 1197 ng/mL for those in the treatment arm, compared to 1147 ng/mL in placebo ($p = 0.88$), and hs-CRP was 176.5 mg/L vs. 244.5 mg/L ($p = 0.39$). P-selectin at 24 h was a mean of 95 ng/mL vs. 99 ng/mL ($p = 0.99$).

Jenab concluded that the study shows increased CRP at 48 h in the colchicine group was less than that in the placebo group, but the difference was not significant.

"Therefore, the study trend was toward the potential benefit for colchicine," he said. The relatively small sample size precludes robust conclusions concerning the study's primary outcome, he added.

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Declaration of competing interest

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