

# Real World Experience of a Biodegradable Polymer Sirolimus-Eluting Stent (Yukon Choice PC Elite) in Patients with Acute ST-Segment Elevation Myocardial Infarction Undergoing Primary Angioplasty: A Multicentric Observational Study (The Elite India Study)

Bhupendra Verma<sup>1\*</sup>, Akhilesh Patel<sup>2</sup>, Deepak Katyal<sup>3</sup>, Vivek Raj Singh<sup>4</sup>, Avinash Kumar Singh<sup>5</sup>, Amrita Singh<sup>1</sup>, Manu Kumar<sup>1</sup>, Pratap Nagarkoti<sup>1</sup>

<sup>1</sup>Department of Cardiology, Ujala Superspeciality Hospital, Kashipur, Uttarakhand, India; <sup>2</sup>Abhigya Heart Care Centre, Gorakhpur, Uttar Pradesh, India; <sup>3</sup>Department of Cardiology, Columbia Asia Hospital, Patiala, Punjab, India; <sup>4</sup>Vardhan Heart Clinic, Varanasi, Uttar Pradesh, India; <sup>5</sup>Department of Cardiology, Khushlok Hospital, Bareilly, Uttar Pradesh, India

## Abstract

**Citation:** Verma B, Patel A, Katyal D, Singh VR, Singh AK, Singh A, Kumar M, Nagarkoti P. Real World Experience of a Biodegradable Polymer Sirolimus-Eluting Stent (Yukon Choice PC Elite) in Patients with Acute ST-Segment Elevation Myocardial Infarction Undergoing Primary Angioplasty: A Multicentric Observational Study (The Elite India Study). Open Access Maced J Med Sci. <https://doi.org/10.3889/oamjms.2019.241>

**Keywords:** BPDES; STEMI; Percutaneous coronary intervention; Third generation stents; Drug-eluting stents; Deliverability; Stent thrombosis

**\*Correspondence:** Bhupendra Verma, Department of Cardiology, Ujala Superspeciality Hospital, Kashipur, Uttarakhand, India. E-mail: [bhupendra.269@gmail.com](mailto:bhupendra.269@gmail.com)

**Received:** 30-Jan-2019; **Revised:** 29-Mar-2019; **Accepted:** 30-Mar-2019; **Online first:** 14-Apr-2019

**Copyright:** © 2019 Bhupendra Verma, Akhilesh Patel, Deepak Katyal, Vivek Raj Singh, Avinash Kumar Singh, Amrita Singh, Manu Kumar, Pratap Nagarkoti. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

**Funding:** This research did not receive any financial support

**Competing Interests:** The authors have declared that no competing interests exist

**BACKGROUND:** The durable polymer drug-eluting stents (DPDES) reduce the risk of repeated target vessel revascularisation (TLR) compared with BMS, but are associated with increased risk of late adverse events. In broadly inclusive populations, the biodegradable-polymer drug-eluting stents (BPDES) have favourable results compared with DPDES in the long term. However, its use in primary angioplasty has not been adequately studied, and data of real-world clinical experience is lacking.

**AIM:** Aim of this study was to assess the safety and efficacy of Yukon Choice PC Elite sirolimus-eluting stent (a novel BPDES) in STEMI patients undergoing primary angioplasty.

**METHODS:** We have presented here one-year clinical follow-up data of the Yukon Choice PC Elite sirolimus-eluting stent in patients undergoing primary angioplasty. A total of 636 patients were enrolled in this single arm, prospective observational study from five centres.

**RESULTS:** This multicentric observational study showed excellent safety and efficacy profile of the novel device at one year follow up. The device-oriented composite endpoint (DOCE) of cardiac death, target-vessel reinfarction, and target-lesion revascularisation (TLR) was 2.7%, and the patient-oriented composite endpoint (POCE) of all-cause death, any myocardial infarction, and any revascularisation was 4.2% at one year. Definite or probable stent thrombosis rate was 0.6%, and no events were recorded beyond 6 months of follow up.

**CONCLUSIONS:** In patients with STEMI undergoing primary angioplasty, the use of Yukon Choice PC Elite (biodegradable polymer sirolimus-eluting stent) has excellent results at one year. It, therefore, represents an attractive alternative to second generation DES in this high-risk population.

## Introduction

Primary percutaneous coronary intervention (PCI) is considered the gold standard of management in ST-segment elevation myocardial infarction (STEMI) [1], [2]. Coronary stenting with a bare-metal stent (BMS) is associated with a lower risk of reinfarction and target vessel revascularisation compared with balloon angioplasty alone [3]. The

advent of drug-eluting stents (DES) has further reduced the in-stent restenosis and the risk of repeated target vessel revascularisation compared with BMS [4]. However, the first-generation DES, including the sirolimus and paclitaxel-eluting stents, have increased the risk stent thrombosis over the long term [5], [6]. These late adverse events are related to hypersensitivity reactions to the durable polymer which produces chronic inflammation and thereby delays endothelial healing and favour stent thrombosis [7], [8], [9]. This is especially important in

patients with STEMI because of plaque rupture, high thrombus burden and increased platelet activation [8], [10]. Moreover, there are chronic processes leading to delayed endothelial healing, vessel remodelling and stent malapposition [8], [11].

Second-generation DES were subsequently developed using thinner stent struts, more biocompatible polymers, and a lower dose of newer anti-proliferative agents (Everolimus and Zotarolimus). The most recent addition to the stent technology is the development of biodegradable polymer drug-eluting stents (BPDES), the third generation DES. These newer generation DES with more biocompatible or biodegradable polymer have been shown to have lower thrombogenicity compared to BMS in experimental studies [12]. However, the ideal DES for use in STEMI is still not clear as there is no conclusive evidence of superiority.

BP-DES degrades after completion of drug release and transforms functionally into BMS. This may improve arterial healing by removing the chronic source of inflammation, the durable polymer, present in all current second-generation DES. Consequently, BP-DES appears to be a novel solution for STEMI, by possibly reducing late ischemic events. We report here the one-year outcomes associated with the use of a novel biodegradable polymer DES, the Yukon Choice PC Elite sirolimus-eluting stent (Translumina Therapeutics, Germany), in STEMI population undergoing primary angioplasty. Recent studies with their use in all-comer populations have been encouraging [13], [14], [15]. However, there is a paucity of data regarding real world experience with this device in STEMI patients.

## Methods

### Patients

This was a prospective observational single arm study from five centres across India. Patients presenting with STEMI were screened for inclusion in the study. Patients were eligible for inclusion if: (1) they presented within 12 hours of symptom onset, or between 12 hours and 24 hours if they had persistent symptoms with evidence of ongoing ischemia; (2) procedures were completed with only Yukon Choice PC Elite DES. Patients were excluded if they had a contraindication to antiplatelet or anticoagulant therapy, undergone CABG, pregnant women and women of childbearing potential and known hypersensitivity to sirolimus, shellac or stainless steel. The study was conducted according to the Helsinki Declaration and the Good Clinical Practice Guidelines. Written informed consent was obtained from each patient before performing the PCI procedure.

### Study Device

The Yukon Choice PC Elite stent is a third generation sirolimus-eluting stent (SES) from Translumina Therapeutics (Germany), now being manufactured in India. This is made up of surgical grade stainless steel (87 µm strut thickness) coated with a biodegradable polymer (polylactic acid, PLA) and sirolimus, which releases from the matrix of Resomer 202S and Shellac resin. It has a unique micro-porous stent surface, PEARL surface, which favours better endothelialisation. The drug is coated only abluminally with no drug or polymer on the luminal side of the stent. Sirolimus eluted from the abluminal side controls smooth muscle cell proliferation, while the luminal side promotes endothelialisation as there is no polymer or drug (acts like BMS). It has the least polymeric load of a biodegradable polymer, 1/4<sup>th</sup> of polymer present in conventional DES. The drug is released in 4-6 weeks, and polymer gets completely degraded in 60-90 days, and it essentially becomes a bare metal stent. Sirolimus has a broad therapeutic profile and flat dose-response curve leading to consistent and homogenous anti-proliferative and immunosuppressant properties. Sirolimus-eluting stents have consistently shown superior outcomes compared to the paclitaxel-eluting stent (PES) [16], [17] and zotarolimus-eluting stent (ZES) [18], whereas comparable safety and efficacy profile to the everolimus-eluting stent (EES) [19], [20]. However, sirolimus is temperature sensitive and get degraded at a temperature of > 30°C into an open-chain isomer (34-hydroxy sirolimus) retaining less than 10% of the immunosuppressive activity [21]. The Yukon Choice PC Elite is a cosmetically improved version of Yukon Choice PC stent, which is specially adapted for conditions of extreme temperatures particularly seen in the tropical regions. It comes with dual packing of the outer polystyrene box and inner aluminium pack. Additionally, it has a highly sensitive temperature monitoring device, the Tag Alert, which uses Sensitech Technology.

### Study procedure

All the patients included in the study underwent loading with ticagrelor 180 mg, aspirin 300 mg and atorvastatin 80 mg in the emergency department and shifted to the catheterisation laboratory. The radial approach was the default access site in all patients undergoing primary angioplasty. During the angioplasty procedure, intravenous unfractionated heparin was used for anticoagulation, and glycoprotein IIb/IIIa inhibitors were used as a bail-out. Thrombosuction was used only in cases with large residual thrombus burden after opening the culprit artery with guidewire or balloon. After the intervention, all patients received aspirin indefinitely and clopidogrel, prasugrel or ticagrelor for at least 12 months. Patients remained in

the hospital for at least 48 h. Blood samples were drawn every 24 h for the determination of cardiac markers, blood cell counts and renal function test. Daily recording of ECG was also performed until discharge.

### Follow up and study endpoints

Clinical follow-up visits were scheduled at day 14 and monthly after that up to one year. Frequent follow-up visits, telephonic conversation, reminder messages (SMS) and frequent group counselling sessions were organised to ensure better drug compliance, drug/dose adjustment and collecting data regarding adverse events. The primary endpoint of the study was device-oriented composite endpoint (DOCE) of cardiac death, target-vessel reinfarction, and target-lesion revascularisation (TLR) and the co-primary endpoint was patient-oriented composite endpoint (POCE) of all-cause death, any myocardial infarction, and any revascularisation at the 30-day, 6 months and 1-year of follow-up. The secondary endpoint of this study was the incidence of definite or probable stent thrombosis at the 30-day, 6 months and 1-year of follow-up. Additional secondary endpoints were major/minor bleeding and TLR rates.

### Definitions

Clinical device success was defined as successful delivery and deployment of the first inserted stent and final diameter stenosis after stenting  $\leq 50\%$  by quantitative coronary angiography or visual assessment. Clinical procedure success was defined as clinical device success without the occurrence of serious cardiac events important for ischemia during hospitalisation. Any death was defined as cardiac unless an unequivocal noncardiac cause could be established. Stent thrombosis was defined as acute ( $< 24$  h), subacute (24 h to 30 days), late ( $> 30$  days to 1 year), and very late ( $> 1$  year). It was further defined as per the ARC definition as definite, possible or probable stent thrombosis [22]. Target lesion revascularisation was defined as any clinically indicated repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion. Major and minor bleeding was defined using the Thrombolysis in Myocardial Infarction (TIMI) bleeding criteria [22]. Obesity was defined as body mass index  $> 25$  kg/m<sup>2</sup> [23].

### Statistical analysis

Descriptive analyses were performed. Categorical variables are expressed as number and percentage of patients. Continuous data are reported as mean  $\pm$  SD.

## Results

### Baseline patient characteristics

A total of 636 patients were enrolled in the study. Clinical follow-up was completed in 634 (99.7%) patients at 30 days, 625 (98.2%) at 6 months, and 618 (97.1%) at 1 year, respectively. By the end of one year follow up 14 patients (2.2%) have died, and 4 patients (0.6%) were lost to follow up. The patient follows up is presented in Figure 1.

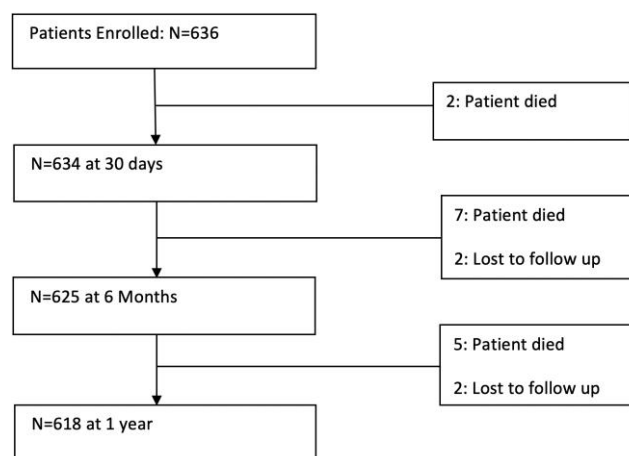


Figure 1: Patient flow and follow up through one year

The mean age was 53.9 years, and 79% of the patients were male. There was a high prevalence of coronary risk factors including hypertension (57.6%), smoking (43.8%), dyslipidaemia (40.8%), obesity (36.9%) and diabetes (20.9%). 3.3% had suffered myocardial infarction before the index event, and 2.8% have earlier undergone PCI. Mean LVEF (left ventricular ejection fraction) was  $\sim 47\%$ . 4.8% of patients presented in cardiogenic shock and 16.9% were in Killip class II or more. Baseline characteristics are shown in Table 1.

Table 1: Baseline patient characteristics (N = 636)

Age (years), mean $\pm$ SD	53.9 $\pm$ 11
Male sex	504 (79.2)
BMI, mean $\pm$ SD	26.5 $\pm$ 6.2
Cardiovascular risk factors	
Obesity	235 (36.9)
Diabetes	133 (20.9)
Hypertension	368 (57.6)
Dyslipidemia	260 (40.8)
Current smoker	279 (43.8)
Family history of CAD	82 (12.8)
Prior MI	21 (3.3)
Prior PCI	18 (2.8)
LVEF, mean $\pm$ SD	46.9 $\pm$ 6.2
Cardiogenic shock	31 (4.8)
Killip class $> 1$	108 (16.9)

### Lesion and procedural characteristics

The mean door to balloon time was 56 minutes. The radial approach was the primary route of angioplasty (96%). LAD/diagonal was the infarct-related artery in half of the patients followed by RCA

(33%), and LMCA constituted 0.9% of the cases. The majority had single vessel disease (69%), and 6.6% had triple vessel disease. The mean diameter and mean length of the stent were 3.14 mm and 26.15 mm, respectively. Multiple stents were used overall in 16% of patients before hospital discharge and in 4% of patients during the index procedure. Direct stenting was done in 67% of the patients. Thrombosuction was used in 3.3% patients, and bailout Gp IIb/IIIa inhibitor use was 10.5%. Clopidogrel (79%) was the most commonly prescribed DAPT (dual antiplatelet therapy) along with aspirin followed by ticagrelor (14%) and prasugrel (7%). Compliance to DAPT at one year was 94%. The device success rate was 99.3%, and the procedure success rate was 98.1%. Lesion and procedural characteristics are summarized in Table 2.

**Table 2: Lesion and procedural characteristics (N = 636)**

Door to balloon (minutes), mean $\pm$ SD	56 $\pm$ 11
Radial access	612 (96.2)
Infarct related artery	
Left main	6 (0.94)
LAD/Diagonal	309 (48.5)
LCX/Marginal	108 (16.9)
RCA	213 (33.4)
Multivessel disease	193 (30.3)
Reference vessel diameter (mm), mean $\pm$ SD	2.91 $\pm$ 0.25
Stented length (mm), mean $\pm$ SD	26.15 $\pm$ 6.35
Stent diameter (mm), mean $\pm$ SD	3.14 $\pm$ 0.28
Stent implanted per patient	1.18 $\pm$ 0.40
Multiple stents used	102 (16)
Thrombosuction	21 (3.3)
Direct stenting	426 (66.9)
Gp IIb/IIIa inhibitor use*	67 (10.5)
DAPT usage	
Clopidogrel	79%
Prasugrel	7%
Ticagrelor	14%
DAPT compliance at 1-year	94%
Device success	99.3%
Procedure success	98.1%

### Clinical outcomes

At one-year clinical follow-up, 14 patients (2.2%) had died, including 9 patients (1.4%) who died of cardiac reasons. The device oriented primary endpoint (DOCE) was seen in 1.1% at 30 days, 2% at 6 months and 2.7% at the end of one year.

**Table 3: Clinical follow up**

Outcomes	30 days	6 months	1 year
All death	3 (0.5)	9 (1.4)	14 (2.2)
Cardiac de	3 (0.5)	7 (1.1)	9 (1.4)
MI (non-fatal)	2 (0.3)	4 (0.6)	5 (0.8)
Target vessel reinfarction	2 (0.3)	3 (0.5)	3 (0.5)
Any revascularization	5 (0.8)	9 (1.4)	11 (1.7)
TLR (clinical driven)	3 (0.5)	5 (0.8)	8 (1.2)
Device oriented endpoint $\beta$	7 (1.1)	13 (2)	18 (2.7)
Patient oriented endpoint $\beta$	9 (1.4)	19 (3)	26 (4.2)
Stent thrombosis *	3 (0.5)	4 (0.6)	4 (0.6)
Definite	2 (0.3%)	2 (0.3%)	2 (0.3%)
Probable	1 (0.15%)	2 (0.3%)	2 (0.3%)
Major and minor bleeding	3 (0.5)	7 (1.1)	9 (1.5)

The patient-oriented co-primary endpoint (POCE) was 1.4%, 3% and 4.2% at 30 days, 6 months and 1 year respectively. The target lesion reinfarction at one year was 0.5%, and the clinical

driven TLR rate was 1.2%. Definite and probable stent thrombosis occurred in 2 patients each till 6 months follow up (total 4 patients, 0.6%). Both of the definite stent thromboses were sub-acute (early stent thrombosis). Beyond 6 months no additional case of stent thrombosis was seen. The major and minor bleeding rates at one year were 1.5%. The clinical outcomes are detailed in Table 3.

## Discussion

To our knowledge, this is the largest study reporting the real-world experience of biodegradable polymer sirolimus-eluting stent in the STEMI population undergoing primary angioplasty. This prospective, observational multicentric study showed excellent safety and efficacy profile of Yukon Choice PC Elite with low rates of POCE, DOCE, TLR and overall stent thrombosis rates at one year follow up. The study cohort had a high prevalence of cardiovascular risk factors, cardiogenic shock and poor Killip class, thereby reflecting real clinical practice and testing the stent in a real-world setting. This novel device with enhanced biocompatibility, therefore, appears to be an attractive option in the STEMI population.

The Yukon Choice PC stent (Translumina therapeutics, Hechingen, Germany) consists of a unique microporous stainless-steel stent surface coated abluminally with sirolimus and a PLA biodegradable polymer. This sirolimus-eluting BP-DES has been found non-inferior to permanent polymer SES (Cypher) in the ISAR-TEST-3 study and permanent polymer EES (XIENCE V) or SES (Cypher) in ISAR-TEST-4 [13], [14]. Outcomes were non-inferior even at 3 years and 5 years follow up [24], [25]. The Yukon stent has also been shown to be non-inferior to the PES in diabetic patients (LIPSIA-Yukon trial) [26], [27]. Furthermore, the ISAR-TEST 5 trial showed that this strut had non-inferior results at one year and five years compared to a zotarolimus-eluting stent [28], [29]. The Yukon Choice PC Elite uses the same stent platform and design as Yukon Choice PC used in the ISAR TEST 3 and 4 trials. The major difference is a temperature control system present with the current device, as sirolimus is temperature sensitive.

We have experienced high device and procedural success rate using the Yukon Elite stent (99.3% and 98.1% respectively). This is comparable to a procedural success rate of 97.5% using EES in EXAMINATION Trial [30]. All the operators in this study report to have experienced exceptional manoeuvrability, deliverability and flexibility during stent deployment. Direct stenting was done in 67%, and it failed in 5.6% patients, which is considerably lower than previously reported with 2<sup>nd</sup> generation

DES (17-18%) [31], [32]. No case of failure of stenting, a mechanical complication related to stent or change over to different DES was seen. Given comparable efficacy of the contemporary DES, deliverability is certainly an important feature in relative superiority of stents. Unfortunately, deliverability data from randomised clinical trials are almost negligible, and therefore real-world experience is critical for determining relative deliverability. The excellent deliverability with Yukon Choice PC stent could be explained by widely spaced, thinner struts (87  $\mu\text{m}$ ) and newer improved stent delivery system.

There are limited studies comparing new-generation DES (n-DES) and BMS in the STEMI population. In the recent two trials-COMFORTABLE AMI trial (biolimus-eluting stent with biodegradable polymer versus BMS) and EXAMINATION trial (EES versus BMS) in STEMI-new-generation DES were convincingly superior to BMS [30], [33]. Meta-analysis of these trials showed a significant reduction in rates of target vessel re-infarction, TLR and stent thrombosis in the DES arm [34]. Moreover, this benefit was extended up to 2-year follow-up in both trials [35], [36]. More recently, the 5-year follow-up of EXAMINATION trial demonstrated a reduction in the patient-oriented endpoints, device-oriented endpoints, stent thrombosis and all-cause mortality with DES [37]. Stenting with new-generation DES is thus recommended over BMS for primary PCI [2]. The results of the present study confirm these findings with a favourable 1-year safety and efficacy profile. The overall mortality at one year (2.2%) was lower as compared to COMFORTABLE AMI (3.2%) and EXAMINATION trial (3.5%), and the cardiac death too was much lower (1.4% vs 2.9% and 3.2% respectively). The DOCE in our study was 2.7% at one year as compared to 4.3% in COMFORTABLE AMI, and 5.5% EXAMINATION trial and the POCE was 4.2% vs 8.4% and 11.9% respectively.

The BP-DES were designed to confer benefit particularly in terms of late adverse events compared to durable polymer DES. This is especially applicable in STEMI, where the risk of stent thrombosis is increased due to high thrombus burden, increased platelet activation and inflammation leading to delayed endothelial healing. Indeed, in a pooled analysis of three trials in STEMI, BP-DES led to significant reduction in TLR rates and trend towards reduction of definite or probable stent thrombosis [38]. In our study, the overall stent thrombosis rate was 0.6% (definite 0.3% and or probably 0.3%), with no event seen beyond 6 months. This was lower compared to 2.5% in COMFORTABLE AMI trial and 0.9% in EXAMINATION trial [30], [33]. In ISAR-5 trial, the incidence of definite/probable stent thrombosis was 1.1% in BPDES group and 1.2% in Zotarolimus arm at one year, and there was no stent thrombosis seen beyond one year [29]. Similarly, in COMFORTABLE AMI trial, there was no case of late definite stent thrombosis [35].

### Study limitations

The strength of this study was a prospective design with a large number of STEMI patients from multiple centres. However, there were several important limitations too. First, it was an observational study, and a head-to-head comparison is required to confirm the safety and efficacy relative to other newer generation DES. Second, the limited follow up of one year does not allow capturing of very late stent thrombosis. However, recent studies with longer follow up in the STEMI population didn't show any stent thrombosis beyond one year [29], [35]. Third, there may have been underreporting of MI and TLR as follow-up angiography, and routine cardiac biomarker estimation was not mandatory. However, asymptomatic MI and restenosis are usually associated with less clinical significance, and it is unlikely that they would have affected the final results of this study.

Furthermore, the excellent follow-up results represent indirect evidence of favourable effects of the stent used in the study. Fourth, the favourable results in our study may have been influenced by a greater proportion of direct stenting, shorter door-balloon time, experienced operators, predominantly radial approach and selective use of thrombosuction. Finally, there are reports to suggest that the incidence of stent thrombosis is relatively low in Asian populations [39] and thereby the results may not apply to other populations.

In conclusion, in patients with STEMI undergoing primary angioplasty, the use of Yukon Choice PC Elite (biodegradable polymer sirolimus-eluting stent) has excellent safety and efficacy profile at one year. It may, therefore, represent an attractive solution in this high-risk population. However, long-term follow is needed to determine safety in terms of very late adverse events.

### References

1. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet*. 2003; 361:13-20. [https://doi.org/10.1016/S0140-6736\(03\)12113-7](https://doi.org/10.1016/S0140-6736(03)12113-7)
2. Verma B, Singh A, Saxena AK, Kumar M. Deflated Balloon-Facilitated Direct Stenting in Primary Angioplasty (The DBDS Technique): A Pilot Study. *Cardiol Res*. 2018; 9(5):284-292. <https://doi.org/10.14740/cr770w> PMID:30344826 PMCID:PMC6188044
3. Nordmann AJ, Hengstler P, Harr T, Young J, Bucher HC. Clinical outcomes of primary stenting versus balloon angioplasty in patients with myocardial infarction: a meta-analysis of randomized controlled trials. *Am J Med* 2004; 116(4):253-262. <https://doi.org/10.1016/j.amjmed.2003.08.035> PMID:14969654
4. Kastrati A, Dibra A, Spaulding C, Laarmann GJ, Menichelli M, Valgimigli M, et al. Meta-analysis of randomized trials on drug-eluting stents vs. bare-metal stents in patients with acute

- myocardial infarction. *Eur Heart J*. 2007; 28(22):2706-2713. <https://doi.org/10.1093/eurheartj/ehm402> PMID:17901079
5. De Luca G, Dirksen MT, Spaulding C, Kelbaek H, Schalij M, Thuesen L, et al. Drug-eluting vs bare-metal stents in primary angioplasty: a pooled patient-level meta-analysis of randomized trials. *Arch Intern Med*. 2012; 172(8):611-621. <https://doi.org/10.1001/archinternmed.2012.758> PMID:22529227
6. Kalesan B, Pilgrim T, Heinemann K, Raber L, Stefanini GG, Valgimigli M, et al. Comparison of drug-eluting stents with bare metal stents in patients with ST-segment elevation myocardial infarction. *Eur Heart J*. 2012; 33:977-87. <https://doi.org/10.1093/eurheartj/ehs036> PMID:22362513
7. Byrne RA, Joner M, Kastrati A. Polymer coatings and delayed arterial healing following drug-eluting stent implantation. *Minerva Cardioangiolog*. 2009; 57(5):567-84. PMID:19838148
8. Nakazawa G, Finn AV, Joner M, Ladich E, Kutys R, Mont EK, et al. Delayed arterial healing and increased late stent thrombosis at culprit sites after drug-eluting stent placement for acute myocardial infarction patients: an autopsy study. *Circulation*. 2008; 118(11):1138-45. <https://doi.org/10.1161/CIRCULATIONAHA.107.762047> PMID:18725485
9. Joner M, Finn AV, Farb A, Mont EK, Kolodgie FD, Ladich E, et al. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. *J Am Coll Cardiol*. 2006; 48:193e202.
10. Gonzalo N, Barlis P, Serruys PW, Garcia-Garcia HM, Onuma Y, Ligthart J, et al. Incomplete stent apposition and delayed tissue coverage are more frequent in drug-eluting stents implanted during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction than in drug-eluting stents implanted for stable/unstable angina: insights from optical coherence tomography. *JACC Cardiovasc Interv*. 2009; 2(5):445-52. <https://doi.org/10.1016/j.jcin.2009.01.012> PMID:19463469
11. Breet NJ, van Werkum JW, Bouman HJ, Kelder JC, Hackeng CM, ten Berg JM. The relationship between platelet reactivity and infarct-related artery patency in patients presenting with a ST-elevation myocardial infarction. *Thromb Haemost*. 2011; 106(2):331-6. <https://doi.org/10.1160/TH10-08-0528>
12. Kollandaivelu K, Swaminathan R, Gibson WJ, Kolachalama VB, Nguyen-Ehrenreich KL, Giddings VL, et al. Stent thrombogenicity early in high-risk interventional settings is driven by stent design and deployment and protected by polymer-drug coatings. *Circulation*. 2011; 123(13):1400-9. <https://doi.org/10.1161/CIRCULATIONAHA.110.003210> PMID:21422389 PMID:PMC3131199
13. Mehilli J, Byrne RA, Wiecek A, Iijima R, Schulz S, Bruskina O, et al. Randomized trial of three rapamycin-eluting stents with different coating strategies for the reduction of coronary restenosis. *Eur Heart J*. 2008; 29(16):1975-82. <https://doi.org/10.1093/eurheartj/ehn253> PMID:18550554
14. Byrne RA, Kastrati A, Kufner S, Massberg S, Birkmeier KA, Laugwitz KL, et al. Angiographic Results: test efficacy of 3 limus-eluting stents I. Randomized, noninferiority trial of three limus agent-eluting stents with different polymer coatings: the Intracoronary Stenting and Angiographic Results: Test Efficacy of 3 Limus-Eluting Stents (ISAR-TEST-4). *Eur Heart J*. 2009; 30(20):2441-9. <https://doi.org/10.1093/eurheartj/ehp352> PMID:19720642
15. Stefanini GG, Byrne RA, Serruys PW, de Waha A, Meier B, Massberg S, et al. *Eur Heart J*. 2012; 33(10):1214-22. <https://doi.org/10.1093/eurheartj/ehs086> PMID:22447805
16. Schömig A, Dibra A, Windecker S, et al. A meta-analysis of 16 randomized trials of sirolimus-eluting stents versus paclitaxel-eluting stents in patients with coronary artery disease. *J Am Coll Cardiol*. 2007; 50:1373. <https://doi.org/10.1016/j.jacc.2007.06.047> PMID:17903638
17. Stettler C, Wandel S, Allemann S, et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. *Lancet*. 2007; 370:937. [https://doi.org/10.1016/S0140-6736\(07\)61444-5](https://doi.org/10.1016/S0140-6736(07)61444-5)
18. Rasmussen K, Maeng M, Kaltoft A, et al. Efficacy and safety of zotarolimus-eluting and sirolimus-eluting coronary stents in routine clinical care (SORT OUT III): a randomised controlled superiority trial. *Lancet*. 2010; 375:1090. [https://doi.org/10.1016/S0140-6736\(10\)60208-5](https://doi.org/10.1016/S0140-6736(10)60208-5)
19. de Waha A, Dibra A, Byrne RA, et al. Everolimus-eluting versus sirolimus-eluting stents: a meta-analysis of randomized trials. *Circ Cardiovasc Interv*. 2011; 4:371. <https://doi.org/10.1161/CIRCINTERVENTIONS.111.963256> PMID:21791671
20. Bangalore S, Kumar S, Fusaro M, et al. Short- and long-term outcomes with drug-eluting and bare-metal coronary stents: a mixed-treatment comparison analysis of 117 762 patient-years of follow-up from randomized trials. *Circulation*. 2012; 125:2873. <https://doi.org/10.1161/CIRCULATIONAHA.112.097014> PMID:22586281
21. Yatscoff RW, Wang P, Chan K, Hicks D, Zimmerman J. Rapamycin: Distribution, pharmacokinetics, and therapeutic range investigations. *Ther Drug Monit*. 1995; 17:666-671. <https://doi.org/10.1097/00007691-199512000-00020> PMID:8588238
22. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, et al. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation*. 2007; 115(17):2344-51. <https://doi.org/10.1161/CIRCULATIONAHA.106.685313> PMID:17470709
23. Misra A, Chowbey P, Makkar BM, Vikram NK, Wasir JS, Chadha D, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. *J Assoc Physicians India*. 2009; 57:163-70. PMID:19582986
24. Byrne RA, Kastrati A, Massberg S, Wiecek A, Laugwitz KL, Hadamitzky M, et al. Biodegradable polymer versus permanent polymer drug-eluting stents and everolimus- versus sirolimus-eluting stents in patients with coronary artery disease: 3-year outcomes from a randomized clinical trial. *J Am Coll Cardiol*. 2011; 58(13):1325-31. <https://doi.org/10.1016/j.jacc.2011.06.027> PMID:21920260
25. Kufner S, Byrne RA, Valeskini M, Schulz S, Ibrahim T, Hoppmann P, et al. Five-year outcomes from a trial of three limus-eluting stents with different polymer coatings in patients with coronary artery disease: final results from the ISAR-TEST 4 randomised trial. *EuroIntervention*. 2016; 11(12):1372-1373. [https://doi.org/10.4244/EIJY14M11\\_02](https://doi.org/10.4244/EIJY14M11_02) PMID:25405657
26. Desch S, Schloma D, Möbius-Winkler S, Erbs S, Gielen S, Linke A, et al. Randomized comparison of a polymer-free sirolimus-eluting stent versus a polymer-based paclitaxel-eluting stent in patients with diabetes mellitus: the LIPSIA Yukon trial. *JACC Cardiovasc Interv*. 2011; 4(4):452-459. <https://doi.org/10.1016/j.jcin.2010.11.016> PMID:21511226
27. Stiermaier T, Heinz A, Schloma D, Kleinertz K, Dänschel W, Erbs S, et al. Five-year clinical follow-up of a randomized comparison of a polymer-free sirolimus-eluting stent versus a polymer-based paclitaxel-eluting stent in patients with diabetes mellitus (LIPSIA Yukon trial). *Catheter Cardiovasc Interv*. 2014; 83(3):418-424. <https://doi.org/10.1002/ccd.25131> PMID:23873579
28. Massberg S, Byrne RA, Kastrati A, Schulz S, Pache J, Hausleiter J, et al. Polymer-free sirolimus- and probucol-eluting versus new generation zotarolimus-eluting stents in coronary artery disease: The intracoronary stenting and angiographic results: Test efficacy of sirolimus- and probucol-eluting versus zotarolimus-eluting stents (ISAR-TEST 5) trial. *Circulation*. 2011; 124:624-632. <https://doi.org/10.1161/CIRCULATIONAHA.111.026732> PMID:21768546
29. Collieran R, Kufner S, Harada Y, Giacoppo D, Cassese S, Repp J, et al. Five-year follow-up of polymer-free sirolimus- and probucol-eluting stents versus new generation zotarolimus-eluting stents in patients presenting with st-elevation myocardial infarction. *Catheter Cardiovasc Interv*. 2017; 89(3):367-374.

<https://doi.org/10.1002/ccd.26597> PMID:27377301

30. Sabate M, Cequier A, I-guez A, Serra A, Hernandez-Antolin R, Mainar V, et al. Everolimus-eluting stent versus bare-metal stent in ST-segment elevation myocardial infarction (EXAMINATION): 1 year results of a randomised controlled trial. *Lancet*. 2012; 380(9852):1482-90. [https://doi.org/10.1016/S0140-6736\(12\)61223-9](https://doi.org/10.1016/S0140-6736(12)61223-9)

31. Barbato E, Marco J, Wijns W. Direct stenting. *Eur Heart J*. 2003; 24:394-403. [https://doi.org/10.1016/S0195-668X\(02\)00802-3](https://doi.org/10.1016/S0195-668X(02)00802-3)

32. Remkes WS, Somi S, Roolvink V, Rasoul S, Ottervanger JP, Gosselink AT, et al. Direct drug-eluting stenting to reduce stent restenosis: a randomized comparison of direct stent implantation to conventional stenting with pre-dilation or provisional stenting in elective PCI patients. *JACC Cardiovasc Interv*. 2014; 7(7):751-8. <https://doi.org/10.1016/j.jcin.2014.02.012> PMID:25060017

33. Räber L, Kelbæk H, Ostojic M, Baumbach A, Heg D, Tüller D, et al. Effect of biolimus-eluting stents with biodegradable polymer vs bare-metal stents on cardiovascular events among patients with acute myocardial infarction: the COMFORTABLE AMI randomized trial. *JAMA*. 2012; 308(8):777-87. <https://doi.org/10.1001/jama.2012.10065> PMID:22910755

34. Sabaté M, Räber L, Heg D, Brugaletta S, Kelbaek H, Cequier A, et al. Comparison of newer-generation drug-eluting with bare-metal stents in patients with acute ST-segment elevation myocardial infarction: a pooled analysis of the EXAMINATION (clinical Evaluation of the Xience-V stent in Acute Myocardial INfArcTION) and COMFORTABLE-AMI (Comparison of Biolimus Eluted From an Erodible Stent Coating With Bare Metal Stents in Acute ST-Elevation Myocardial Infarction) trials. *JACC Cardiovasc Interv*. 2014; 7(1):55-63. <https://doi.org/10.1016/j.jcin.2013.07.012> PMID:24332419

35. Räber L, Kelbæk H, Taniwaki M, Ostojic M, Heg D, Baumbach A, et al. Biolimus-eluting stents with biodegradable polymer

versus bare-metal stents in acute myocardial infarction: two-year clinical results of the COMFORTABLE AMI trial. *Circ Cardiovasc Interv*. 2014; 7(3):355-64.

<https://doi.org/10.1161/CIRCINTERVENTIONS.113.001440> PMID:24847017

36. Sabaté M, Brugaletta S, Cequier A, I-guez A, Serra A, Hernández-Antolín R, et al. The EXAMINATION trial (Everolimus-Eluting Stents Versus Bare-Metal Stents in ST-Segment Elevation Myocardial Infarction): 2-year results from a multicenter randomized controlled trial. *JACC Cardiovasc Interv*. 2014; 7:64-71. <https://doi.org/10.1016/j.jcin.2013.09.006> PMID:24332423

37. Sabate M, Brugaletta S, Cequier A, Iniguez A, Serra A, Jimenez-Quevedo P, et al. Clinical outcomes in patients with STsegment elevation myocardial infarction treated with everolimus-eluting stents versus bare-metal stents (EXAMINATION): 5-year results of a randomised trial. *Lancet*. 2016; 387(10016):357-366. [https://doi.org/10.1016/S0140-6736\(15\)00548-6](https://doi.org/10.1016/S0140-6736(15)00548-6)

38. de Waha A, King LA, Stefanini GG, Byrne RA, Serruys PW, Meier B, et al. Long-term outcomes of biodegradable versus durable polymer drug-eluting stents in patients with acute ST-segment elevation myocardial infarction: a pooled analysis of individual patient data from three randomised trials. *EuroIntervention*. 2015; 10(12):1425-31. <https://doi.org/10.4244/EIJV10I12A247> PMID:24602961

39. Park DW, Park SW, Park KH, Lee BK, Kim YH, Lee CW, et al. Frequency of and risk factors for stent thrombosis after drug-eluting stent implantation during long-term follow-up. *Am J Cardiol*. 2006; 98(3):352-6. <https://doi.org/10.1016/j.amjcard.2006.02.039> PMID:16860022