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CLINICAL RESEARCH

Self-Expanding Versus Balloon-Expandable Stents in Acute Myocardial Infarction: Results From the APPOSITION II Study

Self-Expanding Stents in ST-Segment Elevation Myocardial Infarction

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Objectives This study sought to investigate whether self-expanding stents are more effective than balloon-expandable stents for reducing stent malapposition at 3 days after implantation in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention.

Background Acute myocardial infarction is associated with vasoconstriction and large thrombus burden. Resolution of vasoconstriction and thrombus load during the first hours to days after primary percutaneous coronary intervention may lead to stent undersizing and malapposition, which may subsequently lead to stent thrombosis or restenosis. In addition, aggressive stent deployment may cause distal embolization.

Methods Eighty patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention were randomized to receive a self-expanding stent (STENTYS, STENTYS SA, Paris, France) (n = 43) or a balloon-expandable stent (VISION, Abbott Vascular, Santa Clara, California; or Driver, Medtronic, Minneapolis, Minnesota) (n = 37) at 9 European centers. The primary endpoint was the proportion of stent strut malapposition at 3 days after implantation measured by optical coherence tomography. Secondary endpoints included major adverse cardiac events (cardiac death, recurrent myocardial infarction, emergent bypass surgery, or clinically driven target lesion revascularization).

Results At 3 days after implantation, on a per-strut basis, a lower rate of malapposed stent struts was observed by optical coherence tomography in the self-expanding stent group than in the balloon-expandable group (0.58% vs. 5.46%, $p < 0.001$). On a per-patient basis, none of the patients in the self-expanding stent group versus 28% in the balloon-expandable group presented ≥5% malapposed struts ($p < 0.001$). At 6 months, major adverse cardiac events were 2.3% versus 0% in the self-expanding and balloon-expandable groups, respectively (p = NS).

Conclusions Strut malapposition at 3 days is significantly lower in ST-segment elevation myocardial infarction patients allocated to self-expanding stents when than in those allocated to balloon-expandable stents. The impact of this difference on clinical outcome and the risk of late stent thrombosis need to be evaluated further. (Randomized Comparison Between the STENTYS Self-expanding Coronary Stent and a Balloon-expandable Stent in Acute Myocardial Infarction [APPOSITION II]; NCT01008085) (J Am Coll Cardiol Intv 2012;5:1209–19) © 2012 by the American College of Cardiology Foundation

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Primary percutaneous coronary intervention (PCI) with balloon-expandable stents is a well-established therapy for patients with ST-segment elevation myocardial infarction (STEMI) (1–4). Patients treated with balloon-expandable stents in the setting of an acute coronary syndrome, however, are known to experience a severalfold increased risk for stent thrombosis compared with patients with stable symptoms (5–7).

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PCI in the setting of acute coronary syndromes could predispose to stent thrombosis owing to the large thrombotic burden already present, suboptimal stent expansion to avoid the risk of no-reflow, or stent implantation on a thrombus that eventually disappears leading to malapposition (8). Various studies have emphasized the importance of correct sizing of balloon-expandable stents, in particular in patients with significant thrombotic burden and subsequent vasoconstriction (9–14). The incidence of incomplete stent deployment and undersizing is between 20% and 30% and is even higher when intravascular ultrasound is used as a technique to assess this (9). It has been recently demonstrated that identification of stent undersizing through eyeballing is a strong predictor of stent thrombosis (9); this was caused by severe calcification, high thrombotic burden with subsequent vasoconstriction, or incorrect judgment of the true coronary vessel size by the performing operator (11–14). By contrast, deployment of balloon-expandable stents with oversized balloons and high-pressure inflation can lead to plaque or thrombus disruption and distal embolization; the subsequent occurrence of poor myocardial reperfusion leads to a lack of myocardial salvage with poor short- and long-term clinical outcomes (6).

Abbreviations and Acronyms

ISA = incomplete stent apposition
MACE = major adverse cardiac events
MI = myocardial infarction
MLD = minimal lumen diameter
OCT = optical coherence tomography
PCI = percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction
TIMI = Thrombolysis In Myocardial Infarction

As most STEMI studies involved balloon-expandable stents, little is known about the effect of treatment with self-expanding stents in PCI. Its use in the setting of STEMI carries potential benefits compared with the use of conventional balloon-expandable stents (15,16). The STENTYS Coronary Stent (STENTYS, Paris, France) is a self-expanding nitinol stent. It has a z-shaped design that is linked together by small interconnections that can be disconnected by balloon inflation between the struts to create side branch access.

The ability of this stent to grow in volume in the first hours to days after the procedure allows gentle deployment with less trauma, but also reduces plaque disruption or thrombus dislodgement and thus could lead to less distal embolization. The increase in the STENTYS stent area (+19%) at 3 days after implantation and the absence of malapposed stents seen at 6 months suggest that this device follows the growth of the vessel lumen while vasoconstriction and thrombus are resolving (15).

The aim of the present trial was to investigate whether self-expanding stents are more effective than balloon-expandable stents for reducing stent malapposition at 3 days after implantation in STEMI patients undergoing primary PCI.

Methods

Study design and patient selection. The APPOSITION II (Randomized Comparison Between the STENTYS Self-Expanding Coronary Stent and a Balloon-expandable Stent in Acute Myocardial Infarction) trial was a randomized, international, multicenter, open-label clinical study with blinded assessment of the study endpoints. The study complied with the Declaration of Helsinki. Local institutional ethical committees approved the study protocol and all participating patients provided informed consent.

The study population consisted of patients admitted for STEMI with onset of symptoms <12 h. STEMI was defined as presence of: 1) detection of rise of cardiac biomarkers with a least 1 value above the 99th percentile of the upper reference limit; 2) chest pain >20 min; 3) electrocardiogram changes indicative of new ischemia, including new ST-T changes (ST deviation ≥0.2 mV precordial leads and/or ≥0.1 mV limb leads) or new left

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bundle branch block. Angiographic inclusion criteria were reference vessel diameter ≥2.5 and ≤4.0 mm and target lesion length <30 mm by visual estimate.

Exclusion criteria were: prior thrombolytic therapy; coronary or cardiac intervention or major surgery of any kind within 30 days before the procedure; target vessel supplied by bypass vessel; MI caused by in-stent restenosis or restenosis; cardiogenic shock; previous stent placement within 10 mm of the target lesion; life expectancy <6 months; left ventricular ejection fraction <30%; cardiovascular accident or transient ischemic attack in the last 6 months; known hypersensitivity or contraindication to study medications, cobalt, nickel, or sensitivity to contrast media; serum creatinine level >2.5 mg/dl; unprotected left main coronary disease with >50% stenosis; excessive tortuosity of the target vessel; lesion aorto-ostial or within 5 mm of the origin of the left anterior descending or left circumflex; severely calcified target lesion.

Randomization and treatment. Before PCI, patients who met study selection criteria were 1:1 randomly assigned to receive treatment with a self-expanding stent (STENTYS stent) or a balloon-expandable stent (VISION, Abbott Vascular, Santa Clara, California; or Driver, Medtronic, Minneapolis, Minnesota) using a computer-generated randomization scheme. The choice between the VISION and Driver stent was left to the discretion of the investigator. Thromboaspiration was recommended, but pre-dilation was left to the discretion of the investigator. Intracoronary nitroglycerin was systematically administered after thrombus aspiration to properly evaluate vessel size. Stent disconnection to allow side branch access was recommended if the diameter of the side branch was >2.25 mm with TIMI (Thrombolysis In Myocardial Infarction) flow grade <3, and/or stenosis >50%, and/or dissection >grade B. The STENTYS stent has the feature that allows each strut to be disconnected using a balloon; the investigator could decide to use this feature to create access to a significant side branch and (if needed) deploy a stent in the side branch. In patients assigned to the balloon-expandable arm, the side branch was supposed to be treated (if necessary) using the provisional stent technique. For both treatment groups, the use of post-dilation was recommended if there was a residual stenosis >30%.

All patients received antithrombotic management according to local practice. After the procedure, patients received aspirin (at least 75 mg/day indefinitely) and clopidogrel (75 mg/day for at least 6 months after the procedure).

The STENTYS Coronary Stent available for the study was a self-expanding, nitinol, bare-metal stent with a nominal strut width of 68 μm (Fig. 1). The stent lengths were 22 and 27 mm with diameters suitable for vessels with reference vessel diameters between 2.5 and 3.0 mm (small),

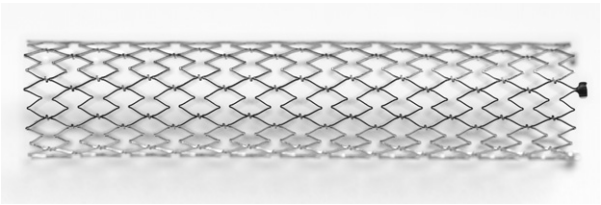

Figure 1. Stentys Self-Expanding Nitinol Stent

3.0 to 3.5 mm (medium), and 3.5 to 4.0 mm (large). The stent could be delivered through a 6-F compatible, rapid-exchange delivery system over a conventional 0.014-inch guidewire.

Follow-up, study endpoints, and definitions. Clinical data were collected before and after the procedure, at discharge, and at 30 days. Angiographic and optical coherence tomography (OCT) assessments were performed immediately after stent implantation and at 3 days after the procedure.

The primary endpoint was strut malapposition at 3 days measured by OCT. Malapposition was defined as the distance between the leading edge of the strut and the leading edge of the contour bigger than the strut thickness. The thickness (defined as the distance between the inner and outer part of the stent strut measured along the radial axis) of the STENTYS stent is 112 μm for the small and 146 μm for the medium and large sizes; the strut thicknesses for the VISION and Driver stents were 84 and 100 μm, respectively.

Secondary endpoints included: major adverse cardiac events (MACE) and component endpoints; target vessel failure; stent thrombosis at 30 days and 6 months; and stent-to–reference lumen diameter ratio.

MACE were defined as cardiac death, recurrent MI, emergent bypass surgery (coronary artery bypass graft), or clinically driven target lesion revascularization by percutaneous or surgical methods. Target vessel failure was defined as cardiac death, target vessel MI (Q- or non–Q-wave), or clinically driven target vessel revascularization by percutaneous or surgical methods.

Angiographic assessment. Quantitative coronary analysis was performed using the CAAS5 analysis system (Pie Medical BV, Maastricht, the Netherlands). In each patient, the stented segment and the peristent segments (defined by a length 5 mm proximal and distal to the stent edge) were analyzed. Quantitative analyses of all angiographic data were performed off-line by an independent core laboratory (Cardialysis, Rotterdam, the Netherlands). Quantitative coronary analysis parameters determined were computer-defined minimal lumen diameter (MLD), reference diameter obtained by an interpolated method, and percentage

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diameter stenosis. Binary restenosis was defined in every segment as diameter stenosis ≥50% at follow-up. Late loss was defined as the difference between post-procedure MLD and MLD at follow-up.

OCT assessment. OCT acquisition was executed with the C7 XR Fourier-Domain System (LightLab Imaging, Westford, Massachusetts) using the flushing technique. The acquisitions were performed advancing the conventional wire distal to the segment of interest. Then, the OCT imaging catheter (RX ImageWire II, LightLab Imaging) was advanced distally to the treated region. Pullback was performed during continuous injection of contrast medium (3 ml/s, iodixanol 370, Visipaque, GE Healthcare, Cork, Ireland) through the guide catheter with an injection pump. In this case, the automated pullback rate was 20 mm/s and the frame rate was 100 images/s.

The OCT measurements were performed with QCU-CMS software (Medis Medical Imaging Systems BV, Leiden, the Netherlands) by an independent core lab (Cardialysis, Rotterdam, the Netherlands). The analyzed region comprised the stented segment and the 5 mm proximal and distal persistent segments. Frames were excluded from the analysis if there was a nonuniform rotational distortion, and if struts and vessel wall could not be visualized due to insufficient blood clearance, presence of intraluminal mass, or insufficiently flushed OCT catheter.

The lumen and stent areas were measured at 1-mm intervals. The lumen contour was obtained with an automated detection algorithm available in the QCU-CMS software and additional manual corrections were performed if necessary. To measure the stent area, the stent contour was traced using a multiple point detection function (17). A support point for the contour was set in the middle of the endoluminal border of each stent strut. A semiautomated contour was then applied linking the points. To define apposition of the struts, the following were performed: 1) The distance from the middle point of the endoluminal side of each strut to the lumen contour was measured. 2) If this distance was longer than the strut thickness, this was considered as a malapposed strut. 3) In the frames with malapposed struts, the incomplete stent apposition (ISA) area was drawn manually; it usually takes a half-moon shape. The ISA area was defined as the space between the lumen contour and the stent contour at the location of malapposed struts. This constituted the ISA area of that frame. To get the mean ISA area per patient, all those ISA areas were summed and divided by the total number of analyzed frames (18). In addition to ISA analyzed at patient level, it was also analyzed at strut level and at malapposition zone level. The axial distance between the strut's surface to the luminal surface was measured. If this was greater than the strut thickness, then a strut was malapposed. Malapposition distance was defined as the distance between the luminal part of the strut minus the strut thickness at ISA strut level. Mean prolapse area was defined as the convex-shaped area of tissue protrusion between adjacent stent struts toward the lumen, without disruption of the continuity of the luminal vessel surface.

Statistical analysis. A total of 72 patients needed to be enrolled to achieve a power of 80%, with a 2-sided significance level of 0.05, to detect a 3.5% absolute difference in the primary endpoint reduction in patients treated with the self-expanding or the balloon-expandable stent. To account for a 10% attrition rate of patients without analyzable OCT at 3 days after implantation, 80 patients (40 in each arm) needed to be included.

The primary analysis sample was based on the principle of intention-to-treat. Statistical analyses were performed by using SAS for Windows (version 9.2, SAS Institute Inc., Cary, North Carolina). Categorical variables were presented as counts and percentages and compared by means of Fisher exact test. Continuous variables are presented as mean ± SD. If the continuous variable could

Table 1. Baseline Clinical and Procedural Characteristics

	Self-Expanding (n = 43)	Balloon-Expandable (n = 37)
Age, yrs	61.7 ± 13.3	59.3 ± 11.6
Male sex	35 (81.4)	29 (78.4)
Diabetes mellitus	7 (16.3)	5 (13.5)
Hypertension	19 (44.2)	19 (51.4)
Hyperlipidemia	19 (44.2)	19 (51.4)
Current smoker	23 (53.5)	26 (70.3)
Prior PCI	0 (0)	0 (0)
Prior CABG	0 (0)	0 (0)
Prior MI	0 (0)	0 (0)
Symptoms onset to PCI, h	3.4 ± 2.5	4.1 ± 2.2
Infarct-related artery		
Left anterior descending	19 (44.2)	12 (32.4)
Left circumflex	5 (11.6)	6 (16.2)
Right coronary artery	19 (44.2)	19 (51.4)
Initial TIMI flow grade 0/1	25 (58.1)	22 (55.0)
Post-PCI TIMI flow grade 0/1	0 (0)*	0 (0)*
Thrombus aspiration	31 (72.1)	31 (83.8)
Stents, n, mean	1.1	1.2
Stents, N	47	44
Pre-dilation	26 (60.5)	15 (40.5)
Post-dilation	27 (62.8)	9 (24.3)
Maximum pressure after dilation, atm	18	20
Diameter of largest balloon, mm	2.78	3.32
Device success	42 (97.6)	37 (100)

Values are mean ± SD or n (%) unless otherwise indicated. *TIMI flow grade 0/1 at 3-days follow-up: 0% (core lab analysis).

CABG = coronary artery bypass graft; MI = myocardial infarction; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

Table 2. Baseline and Follow-Up Quantitative Coronary Analysis

	Self-Expanding (n = 42)*	Balloon-Expandable (n = 40)*	p Value
Pre-procedure			
RVD, mm†	2.82 ± 0.51	2.92 ± 0.42	0.55
MLD, mm‡	0.42 ± 0.55 (0, 0–0.79)	0.47 ± 0.57 (0, 0–0.93)	0.61
DS, %§	85.07 (100, 70–100)	83.76 (100, 68.5–100)	0.77
Lesion length, mm§	13.10 (8.86, 6.85–15.94)	13.97 (15.74, 10.15–16.56)	0.19
Post-procedure			
In-stent MLD, mm†	2.44 ± 0.44	2.70 ± 0.41	0.008
In-stent acute gain, mm†	2.06 ± 0.65	2.25 ± 0.73	0.23
In-stent DS, %‡	15.17 ± 6.67 (14.75, 11.00–19.00)	12.36 ± 4.97 (12.00, 8.00–15.00)	0.054
Stent length, mm‡	21.48 ± 6.48 (19.21, 17.78–23.73)	19.79 ± 5.82 (20.03, 15.36–22.08)	0.23
Follow-up			
In-stent MLD, mm†	2.56 ± 0.48	2.66 ± 0.41	0.32
In-stent DS, %†	14.11 ± 7.78	11.95 ± 6.77	0.19
In-stent lumen loss, mm†	−0.12 ± 0.29	0.04 ± 0.21	0.011

Values are mean ± SD (median, IQR) unless otherwise indicated. *Forty-two of 48 and 40 of 44 stents, respectively, were analyzable by the core lab at baseline and follow-up. †*t* test. ‡*t* test after log transformation. §Median test.

DS = diameter stenosis; IQR = interquartile range; MLD = minimal lumen diameter; RVD = reference vessel diameter.

be considered as normally distributed (alpha = 0.05), a *t* test on the original data was performed. In case the variable could be considered to follow a log-normal distribution (alpha = 0.05), a *t* test on log-transformed data was performed. If also log normality was rejected, we used an ordinal test, being the median test. In case a *t* test was performed, it was Student unpaired *t* test for between-group comparison and the paired *t* test for within-group comparison. The Levene test was used to evaluate the homogeneity of the variances.

For variables representing the per-strut level, however, the p values were calculated by applying a multilevel logistic regression analysis (categorical columns) or a multilevel linear regression model (continuous columns), taking into account the within-patient correlation between the results. For this, the SAS procedures PROC MIXED (continuous variables) and PROC GENMOD (categorical variables) were used.

For all analyses, a 2-sided p value <0.05 was considered statistically significant.

Results

Between December 2009 and June 2010, 80 eligible patients were randomly assigned to receive the self-expanding STENTYS stent (n = 43) or a balloon-expandable stent (VISION or Driver stent, n = 37) in 9 European centers. All patients had a primary PCI procedure with stent implantation and follow-up OCT imaging at 3 days after implantation as required by protocol. There was no significant difference between groups with regard to baseline clinical characteristics (Table 1). In the STENTYS group, 1 patient had a >30% residual stenosis directly after stent placement, which decreased to <30% confirmed by angiography at 3 days. Thrombectomy was performed in 84% of all cases (62 of 80) without significant difference between the self-expanding group (72.1%) and the balloon-expandable group (83.8%). In the self-expanding group,

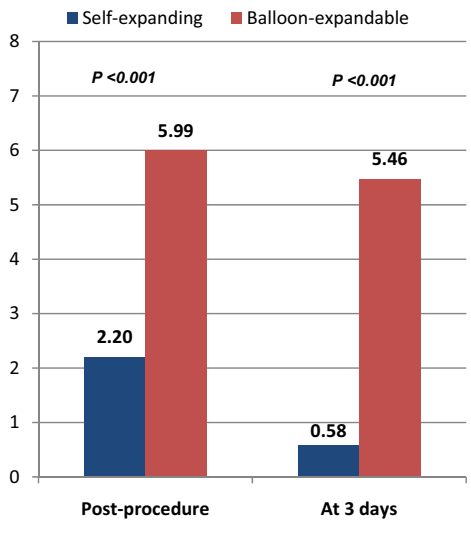

Figure 2. Stent Strut Malapposition After the Procedure and at 3 Days

After the procedure, the percentage malapposed struts in the self-expanding group was lower than in the balloon-expandable group (2.20% vs. 5.99%). Three days later, this difference was even more pronounced: 0.58% in the self-expanding group versus 5.46% in the balloon-expandable stent group.

Table 3. OCT Quantitative and Qualitative Analysis

Post-Procedure	Self-Expanding n = 36	Balloon-Expandable n = 35	p Value
Analysis at patient level			
Struts analyzed, n* (median, IQR)	607 (533, 490–647)	288 (265, 217–323)	<0.001
Lumen area, mm^2†	7.94 ± 2.19	8.92 ± 2.22	0.07
Stent area, mm^2†	8.10 ± 2.21	9.10 ± 2.37	0.07
Lumen volume, mm^3†‡	200.69 (196, 155–245)	208.38 (211, 140–245)	0.84
Stent volume, mm^3‡	205.07 (196, 155–249)	213.26 (222, 134–250)	0.88
ISA area, mm^2‡	0.04 (0.015, 0.002–0.041)	0.14 (0.043, 0.016–0.103)	0.014
Malapposed struts, %§	2.20 ± 3.92	5.99 ± 7.28	<0.001
Mean prolapse area, mm^2†‡	0.20 (0.140, 0.048–0.288)	0.32 (0.295, 0.182–0.428)	<0.001
Frames with ≥1 dissection, %*	0.28 (0, 0–0)	1.29 (0, 0–2)	0.030
Malapposed struts‖	28 (77.8)	34 (97.1)	0.028
Malapposed struts >5%‖	5 (13.9)	13 (37.1)	0.031
Calculated stent length, mm*	25.56 ± 5.77 (24.0, 21.4–26.7)	23.34 ± 6.69 (23.0, 18.4–26.6)	0.90
Analysis at ISA strut level, n	267	588	
Malapposition distance, mm§	0.10 ± 0.17	0.14 ± 0.17	0.93
Analysis at malapposition zone level, n	66	111	
Length of malapposition zone, mm*	1.88 ± 1.88 (1, 1–2)	1.77 ± 1.66 (1, 1–2)	0.87
Follow-up	**n = 40**	**n = 36**	
Struts analyzed*†	584 ± 186 (554, 479–616)	287 ± 104 (248, 222–336)	<0.001
Lumen area, mm^2†	8.99 ± 2.39	8.81 ± 2.18	0.73
Stent area, mm^2‡	9.31 (8.77, 7.42–10.90)	8.93 (8.47, 7.43–9.91)	0.50
Lumen volume, mm^3†‡	227.39 (223, 175–253)	207.28 (201, 147–243)	0.14
Stent volume, mm^3‡	235.51 (234, 184–269)	210.82 (208, 150–249)	0.08
ISA area, mm^2‡	0.02 (0.007, 0–0.035)	0.15 (0.055, 0.023–0.118)	0.009
Malapposed struts, %§	0.58 ± 0.70	5.46 ± 6.98	<0.001
Mean prolapse area, mm^2†‡	0.34 (0.28, 0.15–0.46)	0.27 (0.25, 0.18–0.32)	0.80
Frames with ≥1 dissection, %*	0.40 ± 1.01 (0, 0–0)	0.83 ± 1.52 (0, 0–1)	0.19
Malapposed struts‖	24 (60.0)	35 (97.2)	<0.001
Malapposed struts >5%‖	0 (0)	10 (27.8)	0.001
Calculated stent length, mm*	25.46 ± 5.51 (24.4, 21.4–27.2)	23.43 ± 6.93 (23.1, 18.8–26.6)	0.65
Analysis at ISA strut level, n	118	537	
Malapposition distance, mm§	0.19 ± 0.23	0.19 ± 0.20	0.22
Analysis at malapposition zone level, n	42	104	
Length of malapposition zone, mm*	1.55 ± 1.04 (1, 1–2)	1.81 ± 1.51 (1, 1–2)	0.26

Values are mean ± SD (median, IQR) or n (%) unless otherwise indicated. *Median. †*t* test on original data. ‡*t* test after log transformation. §Multilevel analysis. ‖Fisher exact test (categorical).
ISA = incomplete stent apposition; OCT = optical coherence tomography.

post-dilation was performed in 63% (27 of 43) at mean pressures 14.67 ± 3.09 atm. There were significant differences between study sites. One site never post-dilated, whereas 3 other sites post-dilated in 100% of the cases. In the balloon-expandable group, by definition, all patients received balloon dilation at deployment; the deployment pressure was 14.7 ± 2.7 atm (minimum: 10 atm, maximum: 22 atm). In 24% (9 of 37), additional post-dilation (mean pressure: 16.44 ± 2.40 atm) was performed in the balloon-expandable group, again with difference between the sites (varying between 0% in 4 sites and 50% of the cases). The diameter of the largest balloon used was significantly smaller in the STENTYS group than in the balloon-expandable group (2.78 vs. 3.32 mm, $p < 0.05$).

Clinical outcomes. Clinical follow-up was complete in all patients at 30 days and 6 months. At 30 days, no episodes of MACE, including death, MI, revascularization, or stent thrombosis were observed in either group. At 6 months, 1 target lesion revascularization occurred in the self-expanding group, resulting in no significant differences in MACE between the self-expanding and the balloon expanding groups (2.3% vs. 0%, p = NS).

Quantitative coronary angiography. Pre-intervention angiographic measurements were similar for the self-expanding and the balloon-expandable groups. After the

procedure, in-stent MLD in the self-expanding group was lower than in the balloon-expandable group (Table 2).

At 3 days after implantation, there was a significant difference in in-stent lumen loss values between the 2 groups. In the balloon-expandable stent group, the mean in-stent lumen decreased slightly (0.04 ± 0.21 mm), whereas in the self-expanding group, there was a 0.12-mm growth of the lumen from post-procedure to 3-days follow-up.

OCT analysis. After the procedure, lumen and stent area were smaller in the self-expanding than in the balloon-expandable group ($p = 0.07$) (Table 3). The number of struts analyzed was significantly larger in the self-expanding group than in the balloon-expandable group after the procedure (607 vs. 288, $p < 0.001$) and at 3 days (584 vs. 287, $p < 0.001$); this was due to a higher number of struts circumferentially and more struts per unit of stent length (smaller stent cells) in the self-expanding stent group. After the procedure, on a per-strut basis, a lower percentage of malapposed stent struts was observed in the self-expanding group than in the balloon-expandable group (2.20 ± 3.92% vs. 5.99 ± 7.28%, $p < 0.001$) (Fig. 2, Table 3). On a per-patient basis, 13.9% in the self-expanding stent group versus 37.1% in the balloon-expandable group presented malapposed stents (defined as ≥5% malapposed struts (18) after the procedure.

Three days after the procedure, both lumen and stent area were larger in the self-expanding group than in the balloon-expandable group; these differences were not statistically significant.

In the self-expanding stent group, values for stent area and volume significantly increased after the procedure until 3 days ($p < 0.05$); in the balloon-expandable group, lumen area and volume had slightly decreased (p = NS), whereas stent area and volume had slightly increased (p = NS). The difference in malapposition between the 2 groups that existed immediately after the procedure had become more pronounced, mainly due to a further reduction in the self-expanding stent group: 0.58 ± 0.70% in the self-expanding versus 5.46 ± 6.98% in the balloon-expandable group, $p < 0.001$ (Fig. 2). None of the patients in the self-expanding stent group versus 28% in the balloon-expandable group presented malapposed stents ($p = 0.001$) (Fig. 3). Figure 4 shows the distribution of the malapposition distance following the procedure (Fig. 4A) and at 3 days (Fig. 4B); it shows that post-procedural, serious malapposition happens more frequently ($p < 0.001$) in the balloon-expandable than in the self-expanding group. However, there is no significant difference after 3 days of follow-up ($p = 0.46$).

Figures 5 and 6 provide examples of resolution of malapposition in a self-expanding stent versus persistent malapposition in a balloon-expandable stent.

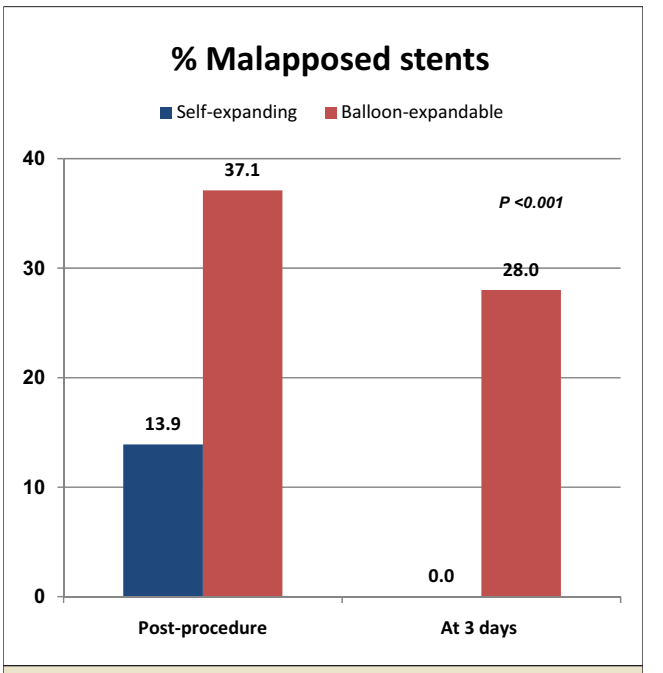

Figure 3. Frequency of Patients With Malapposed Stents (Defined as ≥5% Malapposed Struts)

In the self-expanding stent group, 13.9% of the patients presented with malapposed stents after the procedure, versus 37.1% in the balloon-expandable group. At 3-days follow-up, none of the patients in the self-expanding stent group versus 28.0% in the balloon-expandable group presented malapposed stents ($p < 0.001$).

Discussion

For the first time, a randomized study demonstrates that in patients with acute myocardial infarction undergoing primary PCI, the use of a self-expanding stent, compared with conventional balloon-expandable stents, is associated with significantly better stent strut apposition at 3 days after implantation. In particular, patients treated with balloon-expandable stents had 3× more malapposed struts immediately after the procedure; these differences became more pronounced after 3 days (almost 10× more).

Stent malapposition has been linked with stent thrombosis (12,19). In the intravascular ultrasound substudy of the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial, post-procedural malapposed struts were found in 40.3% of bare-metal stent–treated lesions (20). In the setting of acute myocardial infarction, reasons for early malapposition include adrenergic vasoconstriction leading to underestimation of the reference vessel size, stent underexpansion and recoil, and thrombus dissolution leaving a gap between the stent and the vessel wall (9). By contrast, aggressive stent dilation results in more plaque disruption, embolization, and no-reflow (6).

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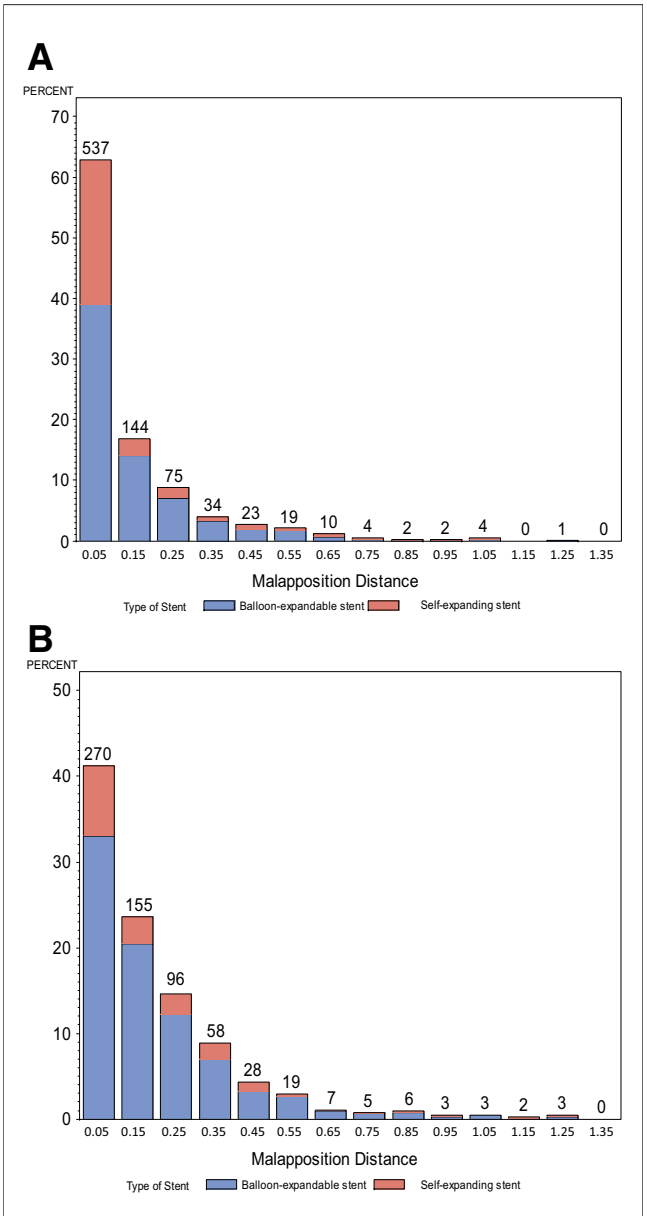

Figure 4. Histograms Presenting Malapposition Distance After the Procedure and at 3 Days

The malapposition distance is defined as the distance (in millimeters) between the strut and the lumen. The numbers and percentages are on incomplete stent apposition struts levels. It shows that post-procedural **(A)** serious malapposition happens relatively more frequently ($p < 0.001$) in the balloon-expandable group than in the self-expanding stent group. However, there is no significant difference after 3-days follow-up ($p = 0.46$) **(B)**.

Previous self-expanding stents showed some shortcomings, such as difficulties in precise positioning and sharp wire ends that could lead to vessel trauma (e.g., Wallstent, Boston Scientific, Natick, Massachusetts) (21), or mechanical properties that did not allow for optimal conformability to vessel wall variations (e.g., Radius stent, Wallstent, Boston Scientific, Natick, Massachusetts) (22). The self-expanding STENTYS stent is a nitinol (nickel-titanium alloy) stent that, upon deployment, exerts a constant, gentle outward force while vasoconstriction and thrombus disappear. The characteristics of self-expanding stents differ from those of balloon-expandable stents. This can be illustrated by assessing the characteristics of the medium-size version of the STENTYS stent, which is used for vessels with reference vessel diameter between 3.0 and 3.5 mm and has an unconstrained diameter of 5.3 mm. The ability to hold the vessel open (the radial force) is virtually identical to the radial force of the Vision stent, but it behaves in a different way. The radial force diminishes only slightly with larger stent diameters (a 16% decrease when the stent diameter increases from 3.0 to 4.0 mm). However, the outward force (the force that puts pressure on the vessel wall—i.e., the chronic outward force) decreases 42% when the stent diameter increases from 3.0 to 4.0 mm. These characteristics allow stent deployment at lower pressures, resulting in less initial barotrauma, and a lower degree of intrastent and edge dissections than are found with balloon-expandable stent use (23). Therefore, it allows slow and gentle expansion of the stent during the first 3 days, an important feature in the initial healing phase of the infarct-related vessel.

The difference in behavior between self-expanding and balloon-expandable stents is reflected in the results of the OCT analysis (Table 3). The stent area in the balloon-expandable group was virtually identical to the lumen area, whereas in the self-expanding group, the stent area was smaller than the lumen area. This is explained by the different type of procedure performed with a self-expanding stent compared with a balloon-expandable stent. Less frequent dilation with smaller balloons under lower mean and maximal pressures performed in the self-expanding group (compared to use of balloons during deployment and additional post-dilation with a balloon-expandable stent) allows the stent to increase gradually its diameter following resolution of spasm and thrombus.

We also found that the post-procedural stent area in the self-expanding stent group was lower than in the balloon-expandable group (8.10 ± 2.21 vs. 9.10 ± 2.37 mm, $p = 0.07$), probably because of the use of smaller balloons under lower pressures in the self-expanding stent group. However, at 3 days after implantation, the stent area in the self-expanding group had increased from 8.10 to 9.31 mm (14.9%, $p < 0.05$); whereas in the balloon-expandable group, the stent area had decreased by 1.9% from 9.10 to 8.93 mm. This is explained by the ability of a self-expanding stent to grow in volume in the first hours to days after a STEMI procedure, following the natural vasodilation of the infarcted vessel in this period.

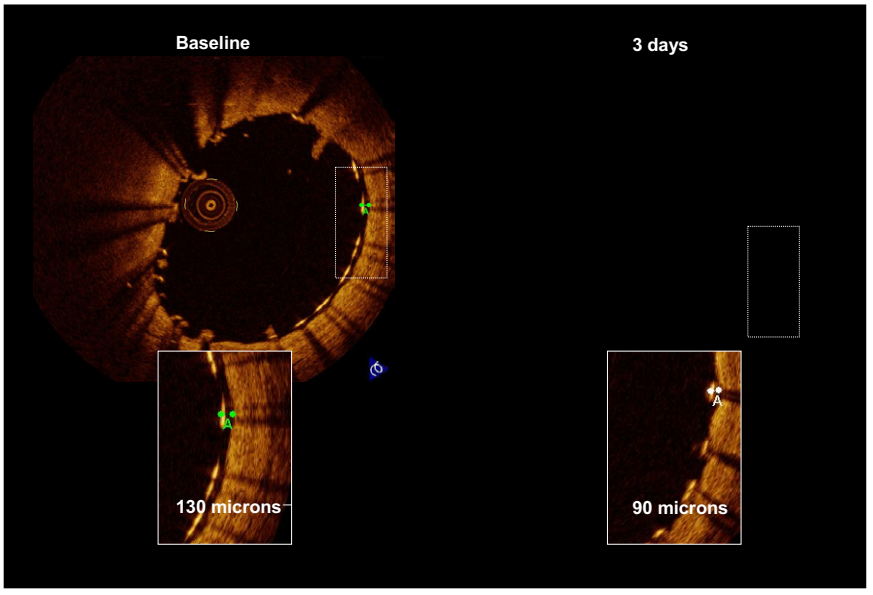

Figure 5. OCT Images of Self-Expanding Stent with Minimal Malapposition Area After the Procedure (Left) and Perfect Apposition at 3 Days (Right)

Optical coherence tomography images of self-Expanding stent with minimal malapposition area after the procedure and perfect apposition at 3-days follow-up.

Similar findings were reported in the APPOSITION I (Assessment of the Safety and Performance of the STENTYS self-expanding Coronary Stent in Acute Myocardial Infarction) trial, a feasibility study assessing the safety and feasibility of the self-expanding stent in 25 patients undergoing primary PCI. At 3-days follow-up, intravascular ultrasound results showed an 18% to 19% increase of mean stent area, minimum lumen area, and mean reference area distal to the stent (15).

To our knowledge, APPOSITION II is the first trial in the setting of STEMI with OCT examinations performed both immediately after stent implantation and at 3 days. OCT has opened up new possibilities for the evaluation of stents, allowing a very detailed assessment of strut apposition (24). Importantly, stent malapposition has been observed lately at 13 months in ~1% of patients undergoing primary PCI with drug-eluting stents (25).

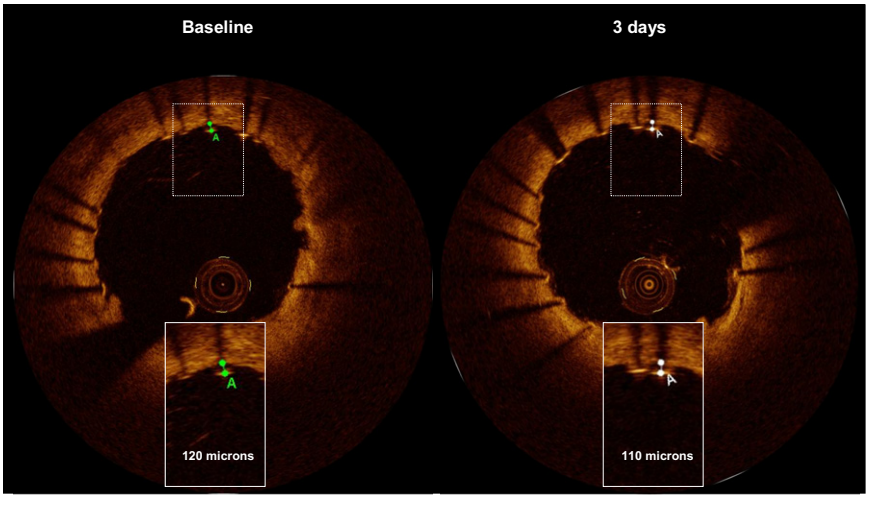

Figure 6. OCT Images of Balloon-expandable Stent with Area of Malapposition After Procedure (Left) and Persistent Malapposition at 3 Days (Right)

Optical coherence tomography images of balloon-expandable stent with area of malapposition after procedure and persistent malapposition at 3-days follow-up.

This finding calls into question current recommendations to prolong the combined use of aspirin and a $P2Y_{12}$ receptor inhibitor for 6 to 12 months after drug-eluting stent placement, while challenging our attempt to define the optimal duration of dual antiplatelet therapy (2). Recent clinical trials, such as the ODESSA (Optical Coherence Tomography for DES Safety) study, have selected OCT variables as their primary endpoint (26). By taking advantage of such OCT features, enough information can be gathered from a relatively small patient cohort to guide the drug and device industry before embarking on large population trials. In this way, we were able to demonstrate that early stent malapposition remains substantially unchanged at 3 days after the procedure when balloon-expandable stents are used. Conversely, as demonstrated by intravascular ultrasound in the APPOSITION I study, the use of a self-expanding stent is associated with increased lumen area and reduced stent malapposition 3 days after deployment. These outcomes may be achieved without requiring the stent to be deployed at high pressures with theoretical benefits in terms of reduced plaque or thrombus dislodgement and less distal embolization (6).

A subanalysis of the LEADERS (Limus Eluted From a Durable Versus Erodable Stent Coating) trial defined a malapposed stent as one with ≥5% struts malapposed (18). Even though this is an arbitrary cutoff percentage, it provides a useful insight in the number of malapposed stents at patient level. When applying this criterion to the APPOSITION II study, it turns out that no patient had malapposed stents in the self-expanding arm, whereas 28% of patients in the balloon-expandable arm did. Whether these benefits may translate into subsequent reduced stent thrombosis and improved clinical outcomes deserves further investigation in larger studies with longer follow-up.

Conclusions

This randomized study in acute MI using OCT as primary endpoint showed for the first time a lower rate of strut malapposition with a self-expanding stent versus a balloon-expandable stent at 3 days after primary PCI. Further studies are needed to assess the clinical significance of improved early stent apposition.

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Key Words: acute myocardial infarction ■ clinical trial information ■ nitinol ■ optical coherence tomography ■ percutaneous coronary intervention ■ self-expanding stents.