Catheterization and Cardiovascular Interventions 84:17–23 (2014)

Performance of the Resolute Zotarolimus-Eluting Stent in Small Vessels

Ronald Caputo,[1*] MD, Martin Leon,[2] MD, Patrick Serruys,[3] MD, PhD, Franz-Josef Neumann,[4] MD, Alan Yeung,[5] MD, Stephan Windecker,[6] MD, PhD, Jorge A. Belardi,[7] MD, Sigmund Silber,[8] MD, PhD, Ian Meredith,[9] MBBS, PhD, Petr Widimský,[10] MD, DrSc, Shigeru Saito,[11] MD, and Laura Mauri,[12] MD, MSc

Background: Drug eluting stents for the treatment of small vessel coronary artery disease have traditionally yielded inferior clinical outcomes compared to the use of DES in large vessels. The benefit of the second-generation Resolute zotarolimus-eluting stent (R-ZES) in small vessels was examined. Methods: Two-year clinical outcomes from five combined R-ZES studies were compared between patients with small (reference vessel diameter [RVD] $\leq$2.5 mm; $n = 1{,}956$) and large (RVD >2.5 mm; $n = 3174$) vessels. Results: Despite a higher incidence of comorbidities in the small vessel group, there was no significant difference in target lesion failure (TLF) (10.1% vs. 8.7%; $P = 0.54$) at 2 years. When the subgroup of patients with diabetes was examined ($n = 1{,}553$) there was no significant difference in 2-year TLF in small compared to large vessels (11.2% vs. 11.1%; $P = 0.17$). Similarly, within the small vessel cohort, no significant difference was seen regarding TLF at 2 years between people with and without diabetes (11.2% vs 9.6%; $P = 0.28$). Conclusion: When used for the treatment of small vessels, the R-ZES appears to provide acceptable clinical results at 2 years when compared to its performance in large vessels.

Key words: coronary artery disease; drug eluting stent; diabetes; small vessel disease

INTRODUCTION

Significant comparative benefits of drug eluting stent (DES) compared to bare metal stent implantation have been convincingly demonstrated. However, in certain subgroups the benefit in regard to a reduction in adverse cardiac events is attenuated. It has been well-established that small reference vessel diameter (RVD) is associated with serious adverse short- and long-term clinical outcomes following implantation of DES [1–3]. While first generation DES have demonstrated clinical benefit compared to bare metal stents in small vessels, these outcomes are still inferior to those seen with DES in the treatment of large vessels [4–8].

[1]St. Joseph's Hospital Cardiology, Liverpool, New York, New York
[2]Cardiovascular Research Foundation, New York, New York
[3]Thoraxcenter-Erasmus University, Rotterdam, The Netherlands
[4]HeartCenter, Universitäts-Herzzentrum Freiburg-Bad Krozingen, Bad Krozingen, Germany
[5]Stanford University School of Medicine, Stanford, California
[6]Bern University Hospital, Bern, Switzerland
[7]Instituto Cardiovascular de Buenos Aires, Buenos Aires, Argentina
[8]Heart Center of the Isar, Munich, Germany
[9]MonashHeart, Monash University, Melbourne, Australia
[10]Cardiocenter, Charles University, Prague, Czech Republic
[11]Shonan Kamakura General Hospital, Kanagawa, Japan
[12]Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts

Conflict of interest: Dr. Caputo has served as consultant and speaker for Medtronic. Dr. Yeung has served as an advisor to Medtronic. Dr. Windecker has received research grant support via institutional grants from Abbott, Biotronik, Boston Scientific, Cordis, Medtronic, and St. Jude Medical. Dr. Belardi has served as a consultant and speaker for Medtronic and Eli Lilly. Dr. Silber has received grant, travel, and analysis support from Medtronic for the RESOLUTE All Comers trial. Dr. Meredith has served as a consultant to Boston Scientific and Medtronic. Dr. Widimský has received occasional speaking honoraria from Medtronic. Dr. Mauri has served as consultant to St. Jude Medical and Biotronik and has received institutional grant support from Abbott, Boston Scientific, Cordis, Medtronic, Eli Lilly, Daiichi Sankyo, Bristol-Myers Squibb, and Sanofi. Drs. Leon, Serruys, Neumann, and Saito have no interests to disclose.

*Correspondence to: Ronald P. Caputo, MD, Director of Cardiac Services, Cardio Lab 2nd Floor, St. Joseph's Hospital, 310 Prospect Ave, Syracuse, NY 13203. E-mail: caputo331@msn.com

Contract grant sponsor: Medtronic, Inc., Santa Rosa, CA, USA.

Received 31 October 2013; Revision accepted 10 March 2014

DOI: 10.1002/ccd.25485
Published online 21 March 2014 in Wiley Online Library (wileyonlinelibrary.com)

Adverse cardiac outcomes following stent implantation are also higher in patients with diabetes, a clinical characteristic that is associated with small RVD [8,9]. To address this problem, second-generation DES have been designed with thinner struts, biocompatible polymers, and antiproliferative drugs with specific elution kinetics [10]. The Resolute™ zotarolimus eluting stent (R-ZES; Medtronic Inc, Santa Rosa, CA) is a second-generation device that has been extensively studied in US and international trials [11–17] and has shown benefit in treatment of patients with diabetes [14,18]. We sought to evaluate the performance of this device in the context of small RVD using the clinical data accrued in these trials.

METHODS

We selected the five Resolute stent studies that had a minimum of 2-year clinical follow-up for analysis—RESOLUTE [11,12] ($n = 139$), RESOLUTE US [13,14] ($n = 1{,}402$), RESOLUTE All Comers [15,16] ($n = 1140$), RESOLUTE International [17] ($n = 2{,}349$), and RESOLUTE Japan ($n = 100$). Briefly, RESOLUTE was a first in man study, RESOLUTE All Comers was a randomized noninferiority study comparing the R-ZES and XIENCE™ everolimus-eluting stent (EES; Abbot Laboratories, Santa Clara, CA) in unrestricted clinical practice, RESOLUTE International was a non-randomized study that excluded only patients with acute ST-elevation myocardial infarction, and RESOLUTE US and RESOLUTE Japan were nonrandomized studies that enrolled according to the inclusion and exclusion criteria associated with product labeling.

The measurement of RVD from the index procedure was performed following the administration of intracoronary nitroglycerin or isosorbide dinitrate according to standard angiographic core lab criteria.

The R-ZES employs a low-profile, thin-strut cobalt alloy platform. The stent elutes zotarolimus from the Biolinx™ tripolymer coating that provides a hydrophilic surface to enhance the biocompatibility of the stent and a hydrophobic component that facilitates the slow release of zotarolimus out to 180 days. The new Resolute Integrity™ (Medtronic Inc, Santa Rosa, CA) iteration uses a continuous sinusoidal design to improve flexibility and deliverability of the stent [19,20].

The studies for this analysis used R-ZES stents with diameters ranging from 2.5 to 4.0 mm. The 2.25 mm diameter R-ZES device was not used. Predilatation of the study lesion was mandatory only in RESOLUTE US and RESOLUTE Japan. High pressure ($\geq$12 atm) stent deployment or postdilatation at high pressure with a non-compliant balloon was encouraged in all cases. Operators were instructed to perform post-dilatation with balloons shorter than the deployed stent. All patients were treated with dual antiplatelet therapy for a minimum duration of 6 months in all studies and continued at the discretion of the operator thereafter.

Endpoints analyzed in this study included cardiac death, target vessel myocardial infarction, and target lesion revascularization. The composite of these individual endpoints comprised the endpoint of target lesion failure (TLF). Deaths were adjudicated as cardiac unless an unequivocal noncardiac cause could be established. The composite endpoints of major adverse cardiac event (death, myocardial infarction, or target vessel revascularization) and target vessel failure (cardiac death, target vessel myocardial infarction, or target lesion revascularization) were also collected. Target vessel myocardial infarction was defined using the extended historical criteria [15]. Definite and probable stent thrombosis was defined using the Academic Research Consortium criteria [21].

All patients were planned to undergo clinical follow-up at 6, 12, and 24 months.

Baseline angiographic data were reviewed by core laboratories in all studies but RESOLUTE International (site-reported and visually estimated). Clinical outcomes were adjudicated by clinical events committees, and safety outcomes were monitored by data monitoring committees. The members of these committees were independent, not directly involved in the studies, and free of conflicts of interest. Academic research organizations coordinated the committees' work, and oversight measures were taken to harmonize definitions across studies in the RESOLUTE Global Clinical Program.

Baseline characteristics were compared between patients with small vessels (RVD $\leq$ 2.5 mm; hereinafter, small vessel group) or without small vessels (RVD $>$ 2.5 mm or missing; hereinafter, large vessel group).

Continuous variables were evaluated using the 2-sample *t*-test. Binary variables were evaluated using Fisher's exact test. Categorical variables were evaluated by Cochran-Mantel-Haenszel modified ridit scores. Propensity scores were calculated with small vessel status as the dependent variable and the following baseline characteristics as independent variables: age, gender, current smoker, prior percutaneous coronary intervention, hyperlipidemia, diabetes, hypertension, prior myocardial infarction, prior coronary artery bypass graft, unstable angina or myocardial infarction, lesion in left anterior descending artery, B2/C lesion, moderate/severe calcification, bend $> 45^{\circ}$, thrombolysis in myocardial infarction score of 3, RVD, lesion length, and % of diameter stenosis. The comparisons of clinical outcomes were adjusted to propensity scores by patients with or without small vessels.

TABLE I. Baseline Characteristics

	Reference Vessel Diameter ≤ 2.5mm ($n = 1956$ patients)	Reference Vessel Diameter > 2.5mm ($n = 3174$ patients)	P value
Age	64.7 ± 10.9	63.3 ± 11.0	<0.001
Male	1397/1956 (71%)	2445/3174 (77%)	<0.001
Diabetes mellitus	672/1956 (34%)	863/3174 (27%)	<0.001
Insulin-dependent	211/1956 (11%)	244/3174 (8%)	<0.001
Hypertension	1506/1956 (77%)	2257/3174 (71%)	<0.001
Hyperlipidemia	1497/1956 (77%)	2173/3174 (69%)	<0.001
Current smoker	409/1956 (21%)	806/3174 (25%)	<0.001
Prior myocardial infarction	529/1940 (27%)	816/3148 (26%)	0.295
Prior percutaneous coronary intervention	648/1956 (33%)	937/3174 (30%)	0.007
Prior coronary artery bypass graft	178/1956 (9%)	261/3174 (8%)	0.281
History of stroke or transient ischemic attack	50/689 (7%)	40/813 (5%)	0.064
Clinical status:			<0.001
Stable angina	773/1956 (40%)	1203/3174 (38%)	–
Unstable angina	522/1956 (27%)	807/3174 (25%)	–
Myocardial infarction	390/1956 (20%)	763/3174 (24%)	–
Silent ischemia	51/1956 (3%)	110/3174 (4%)	–

Values are patients except for age, which is mean years ± standard deviation.

SAS software version 9.1 or later (SAS Institute, Cary, NC) was used for all statistical analyses. P-values <0.05 were considered statistically significant.

RESULTS

A total of 5,130 patients were included in this analysis, of whom 1,956 were in the small vessel group (RVD ≤ 2.5 mm) and 3,174 were in the large vessel group (RVD >2.5 mm). Baseline clinical characteristics differed significantly between these groups (Table I). The patients in the small vessel group were found to be older and more often female. The small vessel group also had a significantly higher incidence of comorbidities such as diabetes, insulin-requiring diabetes, hypertension, and dyslipidemia. Compared with the large vessel group, significantly fewer small vessel patients had prior percutaneous coronary intervention, and fewer were active smokers. Compared with the large vessel group, more patients in the small vessel group were treated for stable and unstable angina and fewer were treated for acute ST-elevation myocardial infarction.

An intergroup comparison of baseline angiographic characteristics (Table II) revealed a baseline RVD of 2.4 ± 0.4 mm in the small vessel group and 3.1 ± 0.4 mm in the large vessel group ($P < 0.001$). There was a higher prevalence of multivessel disease in the small vessel group as well as a higher prevalence of left anterior descending and left circumflex coronary disease (all $P < 0.001$). Lesion length was 14.7 ± 9.2 mm in the small vessel group and 16.5 ± 9.6 mm in the large vessel group ($P < 0.001$). Lesion % diameter stenosis was over 70% by quantitative coronary angiography in both groups.

There was a slightly higher rate of TLF at 2 years in the small vessel group compared to the large vessel group (10.1% vs. 8.7%, adjusted $P = 0.53$) that did not reach statistical significance. Similarly there was no statistically significant difference at 2 years in the individual endpoints of target vessel myocardial infarction, target lesion revascularization, and cardiac death (Table III, Fig. 1). Definite and probable stent thrombosis rates at 2 years were low in both groups (0.8% vs. 1.0%, adjusted $P = 0.29$) with few events occurring after 1 year (0.1% vs. 0.2%, adjusted $P = 0.283$) (Table III).

Intergroup comparisons of small and large vessel patients with diabetes resulted in no statistically significant difference for TLF (11.2% vs. 11.1%, adjusted $P = 0.17$), target lesion revascularization, target vessel myocardial infarction, and cardiac death at 2 years (Fig. 2). Two-year stent thrombosis rates in patients with diabetes were 0.9% in the small vessel group and 1.4% in the large vessel group (adjusted $P = 0.30$). When comparison within the small vessel group was made comparing patients with and without diabetes, the clinical endpoints were similar; the rate of TLF was 11.2% vs. 9.6% in patients with and without diabetes (adjusted $P = 0.28$). Stent thrombosis rates were 0.8% vs. 0.9% (adjusted $P = 0.73$) with only one event in each group after 360 days (Fig. 2).

TABLE II. Baseline Angiographic Characteristics

	Reference vessel diameter ≤ 2.5 mm ($n = 1,956$ patients, 2,974 lesions)	Reference vessel diameter > 2.5 mm ($n = 3,174$ patients, 3,884 lesions)	*P* value
Vessel disease status (>50%), patients			<0.001
Single	590/1217 (49%)	918/1564 (59%)	–
Double	410/1217 (34%)	433/1564 (28%)	–
Triple	207/1217 (17%)	206/1564 (13%)	–
Lesion location, patients			
Left anterior descending artery	1058/1956 (54%)	1478/3174 (47%)	<0.001
Left circumflex artery	809/1956 (41%)	727/3174 (23%)	<0.001
Right coronary artery	554/1956 (28%)	1164/3174 (37%)	<0.001
Left main artery	20/1956 (1%)	75/3174 (2%)	<0.001
Reference vessel diameter, mm	2.4 ± 0.4	3.1 ± 0.4	<0.001
Minimum lumen diameter, mm	0.6 ± 0.4	0.7 ± 0.5	0.002
Lesion length, mm	14.7 ± 9.2	16.5 ± 9.6	<0.001
Mean pre-procedure % diameter stenosis	72.8 ± 16.3	77.7 ± 16.1	<0.001

For RESOLUTE International, angiographic measurements were site-reported. Values are number of units or mean ± standard deviation.

TABLE III. Clinical Outcomes to 2 Years

	Reference vessel diameter ≤ 2.5 mm ($n = 1,912$ patients)	Reference vessel diameter > 2.5 mm ($n = 3,102$ patients)	Adjusted *P* value
Target lesion failure	194 (10.1%)	271 (8.7%)	0.535
Target vessel failure	234 (12.2%)	313 (10.1%)	0.690
Major adverse cardiac events	232 (12.1%)	321 (10.3%)	0.569
Cardiac death or target vessel myocardial infarction	109 (5.7%)	161 (5.2%)	0.488
Death	69 (3.6%)	116 (3.7%)	0.646
Cardiac death	39 (2.0%)	73 (2.4%)	0.668
Target vessel myocardial infarction	75 (3.9%)	98 (3.2%)	0.380
Clinically driven target lesion revascularization	102 (5.3%)	135 (4.4%)	0.341
Clinically driven target vessel revascularization	147 (7.7%)	187 (6.0%)	0.557
Definite/probable stent thrombosis	16 (0.8%)	31 (1.0%)	0.288
Early (≤30 days)	10 (0.5%)	20 (0.6%)	0.550
Late (> 30 days and ≤360 days)	5 (0.3%)	6 (0.2%)	0.360
Very late (>360 days)	2 (0.1%)	5 (0.2%)	0.283

Values are patients. Refer to text for endpoint definitions. *P*-values are adjusted by propensity scores, the independent variables of which are listed in the Methods. *P* value is adjusted to propensity score.

DISCUSSION

Smaller RVD is a variable that has been associated with a higher incidence of adverse angiographic and clinical outcomes following implantation of bare metal stents and first generation DES [1–8]. Second-generation DES have incorporated improvements in scaffold design, polymers, and anti-proliferative drug elution kinetics to achieve improved clinical performance in this higher risk sub-group [10]. In this analysis, the 2-year clinical outcomes following implantation of the second-generation R-ZES were similar in patients with small vessels (RVD ≤ 2.5 mm) compared with those with larger vessels (RVD > 2.5 mm). Similarly, there was no significant difference in the incidence of definite and probable stent thrombosis between groups.

Post hoc and pooled analyses of clinical outcomes following treatment of coronary artery disease with the EES have reported superior outcomes compared to the first-generation paclitaxel-eluting stent (PES) [22,23]. In the SPIRIT III trial, clinical outcomes at 9 months following treatment with a 2.5 mm EES or PES (Taxus™ Express, Boston Scientific Corp, Natick, MA) showed significantly lower rates of major adverse cardiac events primarily related to lower rates of target

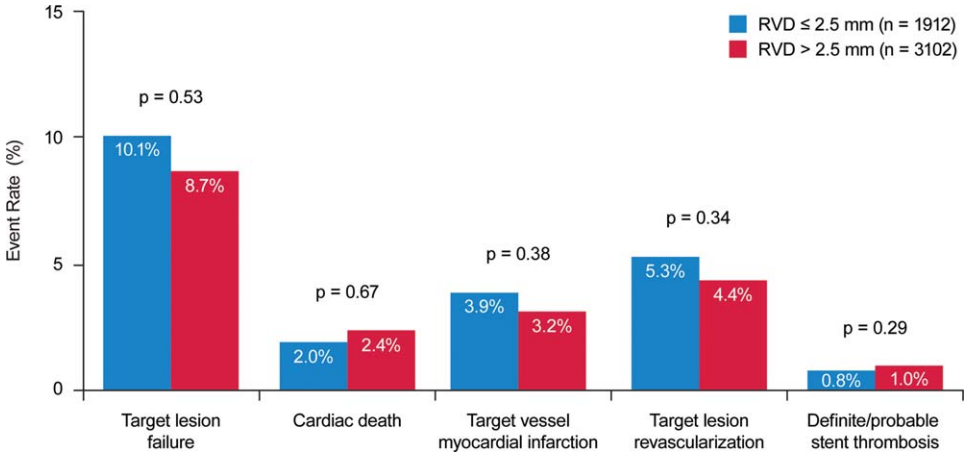

Fig. 1. Comparison of 2-year clinical event rates in small (RVD ≤ 2.5 mm) vs. large vessel (RVD > 2.5 mm) groups. Stent thrombosis was adjudicated according to Academic Research Consortium criteria (Ref. 21). Refer to text for other endpoint definitions. *P*-values are adjusted by propensity scores, the independent variables of which are listed in the Methods. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

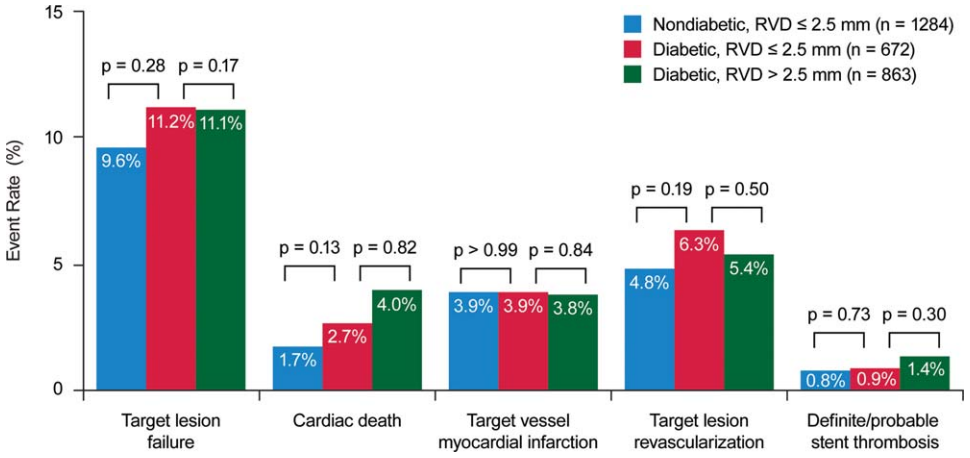

Fig. 2. Comparison of 2-year clinical outcomes in small vessel group (RVD ≤ 2.5 mm) patients with and without diabetes and in small vs. large group (RVD > 2.5 mm) patients with diabetes. Stent thrombosis was adjudicated according to Academic Research Consortium criteria (Ref. 21). Refer to text for other endpoint definitions. *P*-values are adjusted by propensity scores, the independent variables of which are listed in the Methods. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

lesion revascularization (1.3% vs 12.5%, $P = 0.002$) [23]. Longer follow-up is reported in a pooled analysis of three SPIRIT trials plus the COMPARE trial looking at both lesion length and vessel size. In patients with long lesions (length > 13.4 mm) in small vessels (RVD ≤ 2.65 mm) the 2-year rate of major adverse cardiac events was 9.1% for EES and 12.7% for PES. In patients with long lesions or small vessels, major adverse cardiac events were seen in 6.6% and 11.2% of patients receiving an EES or a PES at 2 years. The 2-year rates of major adverse cardiac events were lowest in the patients with larger vessels and shorter lesion length (4.8% and 7.0%) [22]. However none of these patient groups is comparable to the study population reported here (RVD < 2.5 mm with mean lesion length of 14.7 ± 9.2 mm).

A substudy of the LEADERS trial assessed the impact of vessel size on outcomes following treatment with a biolimus-eluting degradable polymer stent (BES; Biomatrix™ Flex, Biosensors Inc, Newport Beach, CA) and a sirolimus-eluting stent (SES; Cypher™ Select, Cordis Corp, Miami Lakes, FL) [24]. Small vessel disease was defined as a RVD ≤ 2.75 mm. In contrast to our data, the rates of major adverse cardiac events (12.1% vs. 7.1%, $P = 0.04$) and target lesion revascularization (9.6% vs. 2.6%, $P = 0.0013$) at

1 year with the BES were significantly greater in patients with small vessels than in those with larger vessels. There was no significant difference in clinical outcomes between the patients with small vessels treated with BES versus SES.

The effect of diabetes, often associated with small vessel diameter, was also examined between the large and small vessel groups as well as within the small vessel group. Compared to patients with diabetes, there was a slightly lower 2-year clinical event rate in patients without diabetes that did not reach statistical significance. Furthermore, among patients with diabetes there was no difference in 2-year clinical events between the large and small vessel groups. No other studies of second-generation DES use in patients with small vessel disease report outcomes in the diabetic subset. These results are consistent with over all outcomes following R-ZES treatment in patients with diabetes [18].

The retrospective design of this study may be considered a limitation. Another potential limitation is the variation in patient inclusion criteria between the studies incorporated in the analysis. However, the uniformity in data collection, follow-up, and end point definitions within these studies organized as part of a comprehensive study program may have attenuated this issue. Our definition of small vessel (angiographic diameter ≤ 2.5 mm) was arbitrary and our data analysis was performed in binomial fashion. These results may not be generalizable to smaller vessels that may be treated with a 2.25 mm stent, which was not available at the time of these studies. Prior studies have suggested a continuous increase in adverse events with decreasing vessel size. Finally, baseline angiographic data—including RVD—for a large proportion of subjects (all those enrolled in RESOLUTE International) were collected via site reports of visual estimation.

Analysis of pooled data from the RESOLUTE global clinical program demonstrates similar 2-year clinical outcomes in large (RVD > 2.5 mm) and small (RVD ≤ 2.5 mm) vessels with the second-generation R-ZES. R-ZES appears to be equally safe and effective in patients with both small and larger vessel diameters including patients with diabetes.

CONCLUSION

Analysis of pooled data from the RESOLUTE global clinical program demonstrates similar 2-year clinical outcomes in large (RVD > 2.5 mm) and small (RVD ≤ 2.5 mm) vessels with the second-generation R-ZES. R-ZES appears to be equally safe and effective in patients with both small and larger vessel diameters including patients with diabetes.

ACKNOWLEDGMENT

Authors thank Minglei Liu, PhD, for statistical analysis oversight and Tim Peoples, MA, ELS, CMPP, and Colleen Gilbert, PharmD. CMPP, for editorial assistance (all of Medtronic).

REFERENCES

1. Kastrati A, Dibra A, Mehilli J, Mayer S, Pinieck S, Pache J, Dirschinger J, Schomig A. Predictive factors of restenosis after coronary implantation of sirolimus- or paclitaxel-eluting stents. Circulation 2006;113:2293–2300.
2. Mehilli J, Dibra A, Kastrati A, Pache J, Dirschinger J, Schomig A, Intracoronary Drug-Eluting Stenting to Abrogate Restenosis in Small Arteries Study I. Randomized trial of paclitaxel- and sirolimus-eluting stents in small coronary vessels. Eur Heart J 2006;27:260–266.
3. Tanimoto S, Daemen J, Tsuchida K, Garcia-Garcia HM, de Jaegere P, van Domburg RT, Serruys PW. Two-year clinical outcome after coronary stenting of small vessels using 2.25-mm sirolimus- and paclitaxel-eluting stents: Insight into the RESEARCH and T-SEARCH registries. Catheter Cardiovasc Interv 2007;69:94–103.
4. Airoldi F, Colombo A, Morici N, Latib A, Cosgrave J, Buellesfeld L, Bonizzoni E, Carlino M, Gerckens U, Godino C, Melzi G, Michev I, Montorfano M, Sangiorgi GM, Qasim A, Chieffo A, Briguori C, Grube E. Incidence and predictors of drug-eluting stent thrombosis during and after discontinuation of thienopyridine treatment. Circulation 2007;116:745–754.
5. Gao R, Abizaid A, Banning A, Bartorelli AL, Dzavik V, Ellis S, Jeong MH, Legrand V, Spaulding C, Urban P. One-year outcome of small-vessel disease treated with sirolimus-eluting stents: A subgroup analysis of the e-SELECT registry. J Interv Cardiol 2013;26:163–172.
6. Habara S, Mitsudo K, Goto T, Kadota K, Fujii S, Yamamoto H, Kato H, Takenaka S, Fuku Y, Hosogi S, Hirono A, Yamamoto K, Tanaka H, Hasegawa D, Nakamura Y, Tasaka H, Otsuru S, Okamoto Y, Yamada C, Miyamoto M, Inoue K. The impact of lesion length and vessel size on outcomes after sirolimus-eluting stent implantation for in-stent restenosis. Heart 2008;94:1162–1165.
7. Hsieh IC, Chien CC, Chang HJ, Chern MS, Hung KC, Lin FC, Wu D. Acute and long-term outcomes of stenting in coronary vessel > 3.0 mm, 3.0–2.5 mm, and < 2.5 mm. Catheter Cardiovasc Interv 2001;53:314–322.
8. Suselbeck T, Latsch A, Siri H, Gonska B, Poerner T, Pfleger S, Schumacher B, Borggrefe M, Haase KK. Role of vessel size as a predictor for the occurrence of in-stent restenosis in patients with diabetes mellitus. Am J Cardiol 2001;88:243–247.
9. Mazeika P, Prasad N, Bui S, Seidelin PH. Predictors of angiographic restenosis after coronary intervention in patients with diabetes mellitus. Am Heart J 2003;145:1013–1021.
10. Biondi-Zoccai G, Moretti C, Abbate A, Sheiban I. Percutaneous coronary intervention for small vessel coronary artery disease. Cardiovasc Revasc Med 2010;11:189–198.
11. Meredith IT, Worthley S, Whitbourn R, Walters DL, McClean D, Horrigan M, Popma JJ, Cutlip DE, DePaoli A, Negoita M, Fitzgerald PJ. Clinical and angiographic results with the next-generation resolute stent system: A prospective, multicenter, first-in-human trial. JACC Cardiovasc Interv 2009;2:977–985.
12. Meredith IT, Worthley SG, Whitbourn R, Walters D, McClean D, Ormiston J, Horrigan M, Wilkins GT, Hendriks R, Matsis P, Muller D, Cutlip DE. Long-term clinical outcomes with the next-generation Resolute stent system: A report of the two-year

follow-up from the RESOLUTE clinical trial. EuroIntervention 2010;5:692–697.
13. Mauri L, Leon MB, Yeung AC, Negoita M, Keyes MJ, Massaro JM. Rationale and design of the clinical evaluation of the Resolute zotarolimus-eluting coronary stent system in the treatment of de novo lesions in native coronary arteries (the RESOLUTE US clinical trial). Am Heart J 2011;161:807–814.
14. Yeung AC, Leon MB, Jain A, Tolleson TR, Spriggs DJ, Mc Laurin BT, Popma JJ, Fitzgerald PJ, Cutlip DE, Massaro JM, Mauri L. Clinical evaluation of the Resolute zotarolimus-eluting coronary stent system in the treatment of de novo lesions in native coronary arteries: The RESOLUTE US clinical trial. J Am Coll Cardiol 2011;57:1778–1783.
15. Serruys PW, Silber S, Garg S, van Geuns RJ, Richardt G, Buszman PE, Kelbaek H, van Boven AJ, Hofma SH, Linke A, Klauss V, Wijns W, Macaya C, Garot P, DiMario C, Manoharan G, Kornowski R, Ischinger T, Bartorelli A, Ronden J, Bressers M, Gobbens P, Negoita M, van Leeuwen F, Windecker S. Comparison of zotarolimus-eluting and everolimus-eluting coronary stents. N Engl J Med 2010;363: 136–146.
16. Silber S, Windecker S, Vranckx P, Serruys PW. Unrestricted randomised use of two new generation drug-eluting coronary stents: 2-Year patient-related versus stent-related outcomes from the RESOLUTE All Comers trial. Lancet 2011;377:1241–1247.
17. Neumann FJ, Widimsky P, Belardi JA. One-year outcomes of patients with the zotarolimus-eluting coronary stent: RESOLUTE International Registry. EuroIntervention 2012;7:1181–1188.
18. Silber S, Serruys PW, Leon MB, Meredith IT, Windecker S, Neumann FJ, Belardi J, Widimsky P, Massaro J, Novack V, Yeung AC, Saito S, Mauri L. Clinical outcome of patients with and without diabetes mellitus after percutaneous coronary intervention with the resolute zotarolimus-eluting stent: 2-Year results from the prospectively pooled analysis of the international global RESOLUTE Program. J Am Coll Cardiol 2013;6: 357–368.
19. Udipi K, Chen M, Cheng P, Jiang K, Judd D, Caceres A, Melder RJ, Wilcox JN. Development of a novel biocompatible polymer system for extended drug release in a next-generation drug-eluting stent. J Biomed Mater Res A 2008;85:1064–1071.
20. Udipi K, Melder RJ, Chen M, Cheng P, Hezi-Yamit A, Sullivan C, Wong J, Wilcox J. The next generation Endeavor Resolute Stent: Role of the BioLinx Polymer System. EuroIntervention 2007;3:137–139.
21. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, McFadden E, Lansky A, Hamon M, Krucoff MW, Serruys PW. Clinical end points in coronary stent trials: A case for standardized definitions. Circulation 2007;115:2344–2351.
22. Claessen BE, Smits PC, Kereiakes DJ, Parise H, Fahy M, Kedhi E, Serruys PW, Lansky AJ, Cristea E, Sudhir K, Sood P, Simonton CA, Stone GW. Impact of lesion length and vessel size on clinical outcomes after percutaneous coronary intervention with everolimus- versus paclitaxel-eluting stents pooled analysis from the SPIRIT (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System) and COMPARE (Second-generation everolimus-eluting and paclitaxel-eluting stents in real-life practice) randomized trials. JACC Cardiovasc Interv 2011;4:1209–1215.
23. Hermiller JB, Fergus T, Pierson W, Su X, Sood P, Sudhir K, Stone GW. Clinical and angiographic comparison of everolimus-eluting and paclitaxel-eluting stents in small coronary arteries: A post hoc analysis of the SPIRIT III randomized trial. Am Heart J 2009;158:1005–1010.
24. Wykrzykowska JJ, Serruys PW, Onuma Y, de Vries T, van Es GA, Buszman P, Linke A, Ischinger T, Klauss V, Corti R, Eberli F, Wijns W, Morice MC, di Mario C, van Geuns RJ, Juni P, Windecker S. Impact of vessel size on angiographic and clinical outcomes of revascularization with biolimus-eluting stent with biodegradable polymer and sirolimus-eluting stent with durable polymer the LEADERS trial substudy. JACC Cardiovasc Interv 2009;2:861–870.