Effect of Optimal Medical Therapy Before Procedures on Outcomes in Coronary Patients Treated With Drug-Eluting Stents

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It has not been established whether the achievement of optimal medical therapy (OMT) before implantation of a drug-eluting stent has a clinical benefit for patients with stable coronary artery disease (CAD). This study included 3,004 patients with CAD treated with drug-eluting stent from 123 Japanese participating centers. The achievement of OMT was defined as control of blood pressure <130/80 mm Hg, hemoglobin A1c <7.0%, and low-density lipoprotein cholesterol <100 mg/dl. The primary end point was target vessel failure, a composite of death related to the target vessel, myocardial infarction, or clinically driven revascularization at 24 months after stent implantation. Immediately before the procedure, only 548 patients (18.2%) had achieved all 3 target criteria (the achieved OMT group), whereas the remaining 2,456 patients failed to achieve one or more criteria (the non-OMT group). At 24 months, the incidence of target vessel failure was 7.0% in the achieved OMT group versus 10.0% in the non-OMT group (hazard ratio 0.68, 95% CI 0.48 to 0.96, p = 0.03). The incidence of non−Q-wave myocardial infarction was also lower in the achieved OMT group than in the non-OMT group (0.5% vs 1.5%, p = 0.08). Multivariate logistic regression analysis identified that hemoglobin A1c <7.0% was the only protective predictor of 24-month target vessel failure (odds ratio 0.56, 95% CI 0.43 to 0.73, p <0.01). In conclusion, this study demonstrated that in patients with stable CAD scheduled for stent implantation, achievement of OMT before percutaneous coronary intervention significantly reduced subsequent cardiac events. Achievement of OMT is still insufficient in modern clinical practice. **(Am J Cardiol 2016;118:790−796)**

Most studies have evaluated the clinical efficacy of potential optimal medical therapy (OMT) for a few years after randomization,[1,2] but no study has assessed whether achieving the goals of an OMT before percutaneous coronary intervention (PCI) reduces subsequent cardiac events. The Japan Drug-Eluting Stents Evaluation: a Randomized Trial (J-DESsERT) is a prospective, randomized controlled study that compares 2 first-generation drug-eluting stents (DESs) for the treatment of coronary artery disease (CAD).[3] In the present study, which is based on data from J-DESsERT, we hypothesized that optimized control of coronary risk factors before PCI may be associated with a risk reduction for perioperative and long-term cardiac events. The present study evaluates whether achievement of all treatment targets improves 24-month outcomes in patients undergoing stent implantation.

Methods

J-DESsERT is a prospective, multicenter, randomized, noninferiority trial that compares 2 first-generation DESs for the treatment of CAD (http://www.clinicaltrials.gov, unique identifier: NCT00708669).[3] A total of 3,533 patients were enrolled from 123 participating centers (See Supplementary Material) from July 2008 to August 2010. The exclusion criteria were as follows: acute myocardial infarction, chronic total occlusion, left main CAD, coronary artery bypass graft disease, or instent restenosis. We also excluded patients who were not available for detailed

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Table 1
Achieved optimal medical therapy versus nonoptimal medical therapy: characteristics of patients and lesions at baseline

Variable	Achievement optimal medical therapy		
	Yes (n = 548)	No (n = 2,456)	p-value
Age (years)	69.8 ± 9.2	69.3 ± 9.2	0.29
Men	417 (76.1%)	1,757 (71.5%)	0.03
Body mass index (kg/m^2)	23.8 ± 3.2	24.5 ± 3.5	<0.01
Hypertension	423 (77.2%)	1,978 (80.5%)	0.09
Dyslipidemia	420 (76.6%)	1,563 (63.6%)	<0.01
Total cholesterol (mg/dl)	158.5 ± 23.2	190.3 ± 34.4	<0.01
Low-density lipoprotein cholesterol (mg/dl)	79.8 ± 16.0	111.6 ± 30.9	<0.01
High-density lipoprotein cholesterol (mg/dl)	51.7 ± 18.3	50.1 ± 13.7	0.02
Triglycerides (mg/dl)	134.6 ± 71.1	142.8 ± 70.9	0.02
Current smoker	90 (16.4%)	470 (19.1%)	0.15
Diabetes mellitus	197 (36.0%)	1,266 (51.6%)	<0.01
Hemoglobin A1c (%)	6.0 ± 0.5	6.8 ± 1.3	<0.01
Prior coronary intervention	140 (25.6%)	541 (22.0%)	0.08
Prior coronary bypass	30 (5.5%)	61 (2.5%)	<0.01
Prior myocardial infarction	96 (17.5%)	323 (13.2%)	0.01
Heart failure hospitalization	30 (5.5%)	113 (4.6%)	0.38
Peripheral arterial disease	34 (6.2%)	198 (8.1%)	0.16
Cerebral vascular disease	61 (11.1%)	306 (12.5%)	0.43
Left ventricular ejection fraction <40%	15 (2.7%)	82 (3.3%)	0.59
Multiple vessel coronary disease	75 (13.8%)	443 (18.1%)	0.02
Paclitaxel-eluting stent	277 (50.5%)	1,217 (49.6%)	0.71
Sirolimus-eluting stent	271 (49.5%)	1,239 (50.4%)	0.71
Narrowings	n = 684	n = 3,193	
Target coronary artery			
Left anterior descending	335 (49.2%)	1,568 (49.2%)	0.88
Left circumflex	160 (23.5%)	725 (22.7%)	
Right	186 (27.3%)	895 (28.1%)	
Type B2/C	436 (64.1%)	2,072 (65.2%)	0.15
Lesion length <10 mm	169 (26.4%)	803 (26.8%)	0.64
Lesion length 10–20 mm	317 (49.6%)	1,427 (47.7%)	
Lesion length ≥20 mm	153 (23.9%)	762 (25.5%)	
Number of deployed stents	1.2 ± 0.4	1.2 ± 0.4	0.38
Stent diameter (mm)	3.0 ± 0.4	3.0 ± 0.4	0.39
Total stent length (mm)	23.0 ± 10.7	24.4 ± 11.7	<0.01
Intravascular ultrasound use	530 (77.5%)	2,434 (76.2%)	0.52
Post-dilation pressure (atm)	17.1 ± 4.2	17.3 ± 4.2	0.46
Technical Success	664 (97.2%)	3,071 (96.2%)	0.22

recording of medical treatments, blood pressure, and key laboratory data such as low-density lipoprotein cholesterol (LDL-C) and hemoglobin A1c levels. After these exclusions, a total of 3,004 patients who underwent PCI were analyzed in this study. In the present study, we set 3 major risk factor targets for patients: LDL-C <100 mg/dl, blood pressure <130/80 mm Hg, and hemoglobin <7% according to guidelines.[4,5] Patients who achieved all 3 target goals at baseline were defined as having achieved OMT. For the control of coronary risk factors, J-DESsERT strongly recommended medical treatment that targeted prespecified values of risk factors: blood pressure, LDL-C, and hemoglobin A1c. Follow-up was scheduled at 30 days and 8, 12, and 24 months after the procedure.[3] Dual

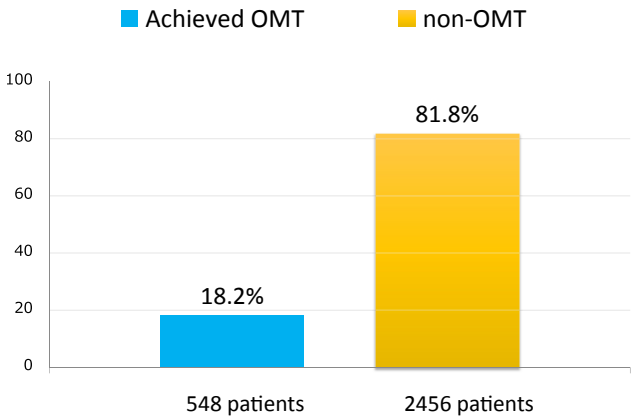

Figure 1. Percentage of patients who achieved OMT *(blue)* and who had non-OMT *(yellow)*.

antiplatelet therapy was recommended for at least 6 months postprocedure and up to 12 months in patients not at a high risk of bleeding. The primary end point of this analysis was the incidence of target vessel failure, a composite of death related to the target vessel, myocardial infarction, or clinically driven target vessel revascularization. Detailed definitions were reported in J-DESsERT's primary publication.[3] Definite and probable stent thromboses were defined by the Academic Research Consortium.[6] All statistical analyses were performed on an intention-to-treat principle. Continuous variables were expressed as mean ± SD and evaluated by means of the Student *t* test. Categorical variables were expressed as frequencies using the chi-square test or Fisher's exact test as appropriate. Time-to-event end points were compared using Kaplan-Meier survival curves, and the corresponding p value was obtained from the log-rank test. Differences between event rates were compared using Cox proportional hazards or logistic regression analyses to estimate the hazard ratio or odds ratio and the 95% CI. To identify independent predictors of 12-month and 24-month target vessel failure, all variables in Table 1 were tested and were also entered into the multivariate logistic regression model. A p value <0.05 was considered statistically significant. Statistical analysis was performed using SAS 9.2 (SAS Institute Inc., North Carolina).

Results

At a point just before the procedure, only 548 patients (18.2%) achieved all 3 targets (Figure 1). The percentage of patients who achieved these target levels were 51.3% (blood pressure), 45.7% (LDL-C), and 73.0% (hemoglobin A1c). Table 1 lists baseline clinical and angiographic characteristics for the patients. Those who achieved OMT (the "achieved OMT" group) were more likely to be men, to have a lower body mass index, and to have dyslipidemia, whereas diabetes mellitus was often observed in patients who did not achieve OMT (the "non-OMT" group). The proportions of the various medications such as statins and antidiabetic drugs therefore differed significantly between the groups (Table 2). Although non-OMT patients also had multiple vessel coronary disease and required a longer stent