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Original Article

Evaluation of Effectiveness and Safety of Everolimus Eluting Stent System (XIENCE V) in the Treatment of Coronary Artery Lesions

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ABSTRACT

Objective: Drug eluting stents have become an important component in percutaneous treatment of patients with symptomatic coronary artery disease. The population in the previous drug eluting stent studies has very risk profile, and therefore not reflects real-world information. Moreover, there are limited data to evaluate risk factors and predictors of intended outcomes. In this study, everolimus eluting stent (XIENCE V) implantations and follow-up results in patients with coronary artery disease were evaluated.

Methods: A total of 833 patients who underwent everolimus eluting stent deployment for coronary artery lesions were enrolled. Baseline demographic, clinic and angiographic data, procedure-related complications, and outcomes during follow-up were studied.

Results: As primary endpoints, all-cause mortality was 1.3% and target lesion failure was 2.3%. As secondary outcomes, cardiac death, target lesion revascularization, target vessel revascularization, myocardial infarction, and stent thrombosis were seen 0.84, 0.8%, 2.2%, 0.6%, and 0.24%, respectively. Premature discontinuation of dual antiplatelet therapy and presentation with acute coronary syndrome were strong predictors for all-cause and cardiac mortality.

Conclusion: Despite heterogeneity and high-risk profile of our patients, procedural-related complications and primary and secondary outcomes were very low with high clinical device and procedure success. These results demonstrate effectiveness and safety of the XIENCE V everolimus eluting stent in a highly complex, real-world patient population.

Keywords: Drug eluting stent, everolimus, coronary artery disease

INTRODUCTION

Drug-eluting stents (DESs) are widely used in the treatment of coronary artery disease (CAD).[1] These stents are coated with antiproliferative drugs, which keep the growth of peripheral intimal and smooth muscle tissue under control and elute drugs for a certain time period.[2] Choice of drug and elution kinetics affects clinical outcomes. Everolimus-eluting stent (EES) systems consist of chrome-cobalt skeleton with thin struts coated with highly biocompatible synthetic fluoropolymers.[3] Many studies have demonstrated better angiographic results with EESs than other DESs.[4,5]

The aim of this study was to determine effectiveness and reliability of stents, especially new-generation stents, which are essential tool of interventional cardiology. Examination of endpoints of myocardial infarction (MI) and stent thrombosis, which can emerge during clinical follow-up of patients in whom stent is implanted, was conducted, and mortality data and relevant effective and/or predictive factors were analyzed.

METHODS

Study Design and Study Population

This single-center, observational, retrospective study was conducted with a total of 1,052 patients aged >18 years who had EES implanted. Patients with symptomatic CAD and signs suggestive of myocardial ischemia on myocardial perfusion scan performed following the positive exercise stress test or those with ≥70% coronary artery lesion detected in conventional angiography performed following the detection of hemodynamically significant stenosis on computed tomography (CT) angiogram were enrolled. Information about the patients was retrieved from hospital files, medical records, laboratory results, and computerized database of angiography laboratory. In addition to basic demographic characteristics of age and gender, accompanying diseases were recorded. Patients who had contraindication for dual antiplatelet treatment (DAPT) consisting of acetylsalicylic acid and clopidogrel, and patients with high probability of undergoing surgical intervention within 6 months

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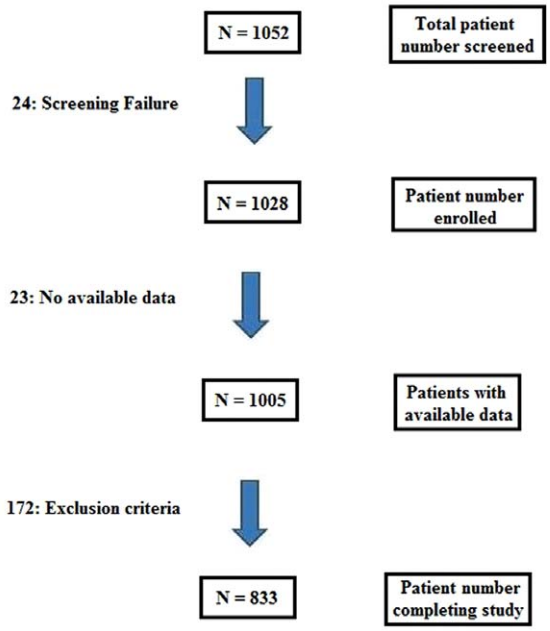
Figure 1. Flow chart of the study design.



were excluded.[6] Patients who had malignancy with life expectancy of <1 year were also excluded. Eventually, 219 patients were excluded, and the study was carried out with 833 patients (Figure 1). The present study was conducted in accordance with the Declaration of Helsinki, and ethics committee approval was received for this study from the ethics committee of Hacettepe University (2013:16969557-1200).

Interventional Procedure, Medical Treatment, and Follow-Up

Everolimus-eluting Xience V stent (Abbott Vascular, Inc., Temecula, CA, USA), with a cobalt-chrome stent platform coated with everolimus was used. In order to avoid vascular overlapping or shortening, severe lesion (vascular luminal stenosis >70%) angiogram with at least two views was displayed. Graft was implanted on lesion according to previously determined nominal pressure recommended by manufacturer and standard coronary angioplasty procedure. Decision to dilate before or after procedure was determined based on physician's preference.

Main Points

- Everolimus eluting stents are clinically effective, reliable, and safe treatment of coronary artery lesions in a patient population with a very heterogeneous clinical spectrum.
- Premature discontinuation of dual antiplatelet therapy and clinical presentation with ACS are associated with unfavorable outcomes including all-cause and cardiac mortality.
- Although male gender is a predominant risk factor for atherosclerosis and clinical cardiovascular disease, female gender was demonstrated to be a risk factor for all-cause and cardiac mortality. In addition, many cardiovascular risk factors were more common in female patients.

Prior to procedure, when performed under elective conditions, any previously prescribed acetylsalicylic acid and/or clopidogrel treatment was administered at daily dose. For patient who had not received acetylsalicylic acid and/or clopidogrel earlier, loading oral dose of acetylsalicylic acid (300 mg) and clopidogrel (600 mg) was administered. During angiography, intravenous bolus dose of heparin (70-100 U/kg) was delivered. Patients with acute coronary syndrome (ACS) were also given loading dose of acetylsalicylic acid (300 mg) and clopidogrel (600 mg) and intravenous bolus dose of 70-100 U/kg heparin during angiography.

After the procedure, patients were monitored continuously in the coronary intensive care unit, and electrocardiographic examination and blood pressure measurements were performed. Patients were followed-up at 1st, 6th, and 12th month after stent implantation, and then at yearly intervals. Need to maintain DAPT for at least 12 months was explained to all patients while in the hospital.[6] Compliance with DAPT was questioned during follow-up visits, and importance of this treatment was stressed by the physician.

Information about patient survival was retrieved from national Death Reporting System (www.obs.gov.tr) with a national ID number of the patient and patient hospital file number.

Endpoints and Definitions

All definitions and endpoints are based on definitions formulated by Academic Research Consortium.[7] Primary endpoints were all-cause mortality and target lesion failure (TLF) as a composite endpoint incorporating MI, target lesion revascularization (TLR), and cardiac mortality. Secondary endpoints were cardiac mortality, MI, TLR, target vessel revascularization (TVR), and stent thrombosis.

Statistical Analysis

Statistical evaluation was performed using the Statistical Package for the Social Sciences version 20.0 (IBM SPSS Corp.; Armonk, NY, USA) and MedCalc 11.4.2 (MedCalc Software, Ostend, Belgium) software. Normal distribution was assessed using Kolmogorov–Smirnov test. Numerical variables with normal and non-normal distribution were displayed using mean ± standard deviation and median, respectively. Categorical variables were indicated as numbers and percentages. For intergroup comparisons of numerical variables with normal distribution, the t-test was used, and for those with non-normal distribution, independent samples t-test and Mann–Whitney U test were applied. Chi-square test and Fisher's exact chi-square test were used to compare pairwise categorical data. To determine the effects of risk factors associated with all-cause and cardiac mortality, the multivariate Cox regression analysis was used to identify independent predictors following the univariate Cox regression analysis. Kaplan–Meier analysis was employed to demonstrate the correlation between endpoints and risk factors during monitoring period. $P < .05$ was accepted as level of significance with 95% confidence interval and 5% standard error.

RESULTS

Baseline Demographic Characteristics

Baseline demographic characteristics of the patients are provided in Table 1. A total of 833 patients (male: n = 621, 74.5%;

Table 1. Baseline Demographic Characteristics of All Study Populations (n = 833)

Age (year)	62.1 ± 10.3
Gender	
Female	212 (25.5%)
Male	621 (74.5%)
Hypertension	522 (62.7%)
Diabetes mellitus	256 (30.7%)
Hyperlipidemia	361 (43.3%)
Family history of coronary artery disease	186 (22.3%)
Smoking habitus	
Non smoker	624 (74.9%)
Ex smoker	58 (7.0%)
Active smoker	151 (18.1%)
Peripheral artery disease	44 (5.3%)
Cerebrovascular disease	25 (3.0%)
Systolic dysfunction	123 (14.8%)
Atrial brillation	60 (7.2%)
Chronic kidney disease	22 (2.6%)
Chronic obstructive pulmonary disease	42 (5.0%)
Malignancy	45 (5.4%)

female: n = 212, 25.5%) were enrolled. Mean age of the patients was 62.1 ± 10.3 years. Female patients were older than male patients (66.1 ± 10.2 vs. 60.8 ± 9.9; $P = .001$). Cardiovascular risk factors diabetes mellitus (DM) (41.0% vs. 27.2%; $P = .001$) and hypertension (HT) (75.9% vs. 58.1%; $P = 0.001$) were significantly more common in women, while the incidence of other accompanying diseases was similar in both groups. The percentage of active and previous smokers was higher among male population compared with female patients (29.3% vs. 6.6%; $P = .001$).

Information about the history of CAD and presenting symptoms is shown in Table 2. Nearly half (48.5%) of the patients had no history of CAD. A great majority (84.9%) of the stent-implanted patients underwent coronary angiography under elective conditions, while 126 patients (15.1%) presented to the clinic with ACS.

Table 2. Information Regarding History of Coronary Artery Disease and Presenting Symptoms of All Study Populations (n = 833)

Previous coronary artery disease	
None	404 (48.5%)
Atherosclerotic heart disease	64 (7.7%)
Percutaneous coronary intervention	211 (25.3%)
Coronary artery bypass operation	154 (18.5%)
Presentation	
Elective admission, positive results of	707 (84.9%)
Ischemic symptoms	476 (57.1%)
Treadmill testing	70 (8.4%)
Coronary computed tomography angiography	129 (15.5%)
Myocardial perfusion scintigraphy	32 (3.8%)
Acute coronary syndrome	126 (15.1%)

Characteristics of Stents and Lesions

A total of 1,134 stents were implanted. The number of EES for each individual was as follows: 1 (n = 587; 70.5%), 2 (n = 199; 23.9%), 3 (n = 39; 4.7%), and 4 (n = 8; 1.0%). Stents were available in 6 diameters, ranging from 2.25 mm to 4.00 mm, and the mean diameter was 2.86 ± 0.38 mm. Stent with a diameter of 2.75 mm was implanted most frequently (28.2%). Stents of 2.50 mm and 3.00 mm in diameter were implanted in 22.9% and 21.6% of the patients, respectively. The mean stent length was 20.4 ± 6.2 mm (range: 8-38 mm). The 18-mm stent was most commonly implanted (31.5%), while the 15-mm and 23-mm stents were used in 19.8% and 18.8% of the patients, respectively.

Characteristics and localization of 1,134 lesion are shown in Table 3. The mean length and diameter of lesion were 18.0 ± 5.9 mm and 2.65 ± 0.35 mm, respectively. Stent implantation was performed for 13 different native or grafted vessels in this study. Most frequently, the left anterior descending artery (45.7%) was the target, followed by right coronary artery (27.6%) and circumflex artery (16.6%). A total of 15 bifurcation lesions and seven ostial lesions were found.

Endpoints and Follow-Up

Endpoints and other events seen during the follow-up period are shown in Table 4. A median follow-up period of the study was 16 months (range: 1-70 months). Among the 833 patients, all-cause and cardiac mortality were seen in 11 (1.3%) and seven (0.84%) patients, respectively. As a primary endpoint, TLF was seen in 19 (2.3%) patients. As a secondary endpoint, TLR (n = 7; 0.8%), TVR (n = 18; 2.2%; total stenosis rate: 3.0%), MI (n = 5; 0.6%), and stent thrombosis (n = 2; 0.24%) were observed in indicated number of patients. None of the patients were transferred to department of cardiovascular surgery during short- or long-term monitoring period.

Table 3. Characteristics and Localization of Coronary Lesions (n = 1,134)

Lesion length (mm)	18.0 ± 5.9
Lesion diameter (mm)	2.65 ± 0.35
Lesion localization	
Left anterior descending artery	518 (45.7%)
Circumex artery	188 (16.6%)
Right coronary artery	313 (27.6%)
Obtuse marginalis	41 (3.6%)
Intermediate artery	11 (1%)
Diagonal branch	29 (2.6%)
Left main coronary artery	8 (0.7%)
Saphenous—right coronary artery graft	11 (1%)
Saphenous—obtuse marginalis graft	4 (0.4%)
Radial—obtuse marginalis graft	1 (0.1%)
Saphenous—left anterior descending artery graft	4 (0.4%)
Saphenous—diagonal graft	4 (0.4%)
Left internal mammary artery graft	2 (0.2%)
Bifurcation lesion	15 (1.3%)
Osteal lesion	7 (0.6%)

Table 4. Study Endpoints (n = 833)

Mortality	
All cause mortality	11 (1.3%)
Cardiac death	7 (0.84%)
Target lesion failure	19 (2.3%)
Target lesion revascularization	7 (0.8%)
Target vessel revascularization	18 (2.2%)
Myocardial infarction	5 (0.6%)
Stent thrombosis	2 (0.24%)
Premature discontinuation of dual antiplatelet therapy	11 (1.3%)
Hospitalization	
Heart failure acute decompensation	17 (2%)
Atrial brillation	12 (1.4%)
Device therapy	
Pacemaker	15 (1.8%)
Implantable cardioverter debrillator	11 (1.3%)
Cardiac resynchronization therapy	8 (1%)

The patients were also classified according to severity and timing of stent thrombosis. One case each of acute and subacute stent thrombosis was seen. Stent thrombosis was observed in 0.17% of 1,134 stents implanted. During the follow-up period, 11 (1.3%) patients discontinued DAPT prematurely.

All-Cause Mortality

Eleven (1.3%) deaths were seen in total of 833 patients. Seven patients died due to cardiac causes, and four cases were all-cause mortality (Table 5). Mean age of patients who died was higher than that of those who survived (75.7 ± 15.2 vs. 62.0 ± 10.1; $P = .013$). In women, who generally have lower risk of CAD, all-cause mortality was more common and finding was significant when compared with male patients (2.8% vs. 0.8%; $P = .036$). History of CVD was more frequently observed in deceased patients relative to those who survived (18.2% vs. 2.8%; $P = .003$). The presence of CKD was more often seen in patients who deceased (18.2% vs. 2.4%; $P = .001$). In 45.5% of the deceased patients, the EF ≤ 50% was observed, while the corresponding percentage was only 14.4% in those who survived ($P = .014$). Average EF of the deceased and surviving patients was estimated at 49% and 60%, respectively. Admission symptoms also differed markedly. Nearly half (45.5%) of those who deceased, but only 14.7% of surviving patients, presented with clinical manifestations of ACS ($P = .010$). Premature discontinuation of DAPT was more frequently and markedly detected among patients who deceased (36.4% vs. 0.9%; $P = .001$). History of other known risk factors, such as DM and CAD, was not found to be correlated with mortality rate ($P > .05$). AF was more frequently detected among patients who deceased without any statistically significant intergroup difference (18.2% vs. 7.1%) ($P = .185$).

In multivariate Cox regression analysis that is used to analyze the effects of significant risk factors detected in univariate regression analysis, increase in age (1.1-fold; 95% CI, 1.064-1.219; $P = .001$), premature discontinuation of DAPT (48-fold; 95% CI, 11.019-216.429; $P = .001$) (Figure 2), and admission with clinical manifestations of ACS (4.6-fold; 95% CI, 1.077-19.914; $P = .039$) (Figure 3) increased all-cause mortality rate as indicated in parentheses.

Cardiac Mortality

Among the 833 patients, cardiac mortality was seen in only seven (0.8%) patients (Table 5). Mean age of the patients who exited due to cardiac causes was significantly higher than that of those who survived (80.5 ± 13.7 vs. 62.0 ± 10.1; $P = .001$). Cardiac mortality was also more commonly seen among female patients. Cardiac mortality was seen in five (2.3%) female and two (0.32%) male patients ($P = .014$). A total of 71.4% of cardiac mortality was in female patients, who constituted only 25.5% of all study population.

Peripheral artery diseases (PADs) and CVD were more frequently detected in patients who died of cardiac causes when

Table 5. Clinical Characteristics of the Patients in Terms of Mortality (n = 833)

	Alive (n = 822)	All cause death (n = 11)	Cardiac death (n = 7)	P*	P†
Age	62.0 ± 10.1	75.7 ± 15.2	80.5 ± 13.7	0.013	0.001
Gender, male	616 (74.9%)	5 (45.5%)	2 (28.6%)	0.036	0.014
Hypertension	512 (62.3%)	10 (90.9%)	6 (85.7%)	0.061	0.266
Diabetes mellitus	254 (30.9%)	2 (18.2%)	1 (14.3%)	0.518	0.683
Hyperlipidemia	357 (43.4%)	4 (36.4%)	3 (42.9%)	0.765	0.976
Family history of CAD	185 (22.5%)	1 (9.1%)	1 (14.3%)	0.472	0.604
Smoking habitus				0.655	0.719
Nonsmoker	615 (74.8%)	9 (81.8%)	6 (85.7%)		
Exsmoker	58 (7.1%)	-	-		
Active smoker	149 (18.1%)	2 (18.2%)	1 (14.3%)		
Peripheral artery disease	42 (5.1%)	2 (18.2%)	2 (28.6%)	0.111	0.006
Cerebrovascular disease	23 (2.8%)	2 (18.2%)	2 (28.6%)	0.003	0.001
Systolic dysfunction	118 (14.4%)	5 (45.5%)	2 (28.6%)	0.014	0.269
Atrial brillation	58 (7.1%)	2 (18.2%)	-	0.182	0.466
Chronic kidney disease	20 (2.4%)	2 (18.2%)	1 (14.3%)	0.001	0.047
COPD	41 (5%)	1 (9.1%)	1 (14.3%)	0.436	0.306
Malignancy	43 (5.2%)	2 (18.2%)	-	0.115	0.534
Previous CAD				0.461	0.326
None	396 (48.2%)	8 (72.7%)	5 (71.4%)		
Atherosclerotic	64 (7.8%)	-	-		
PCI	210 (25.5%)	1 (9.1%)	-		
CABG	152 (18.5%)	2 (18.2%)	2 (28.6%)		
Presentation				0.016	0.038
Elective	701 (85.3%)	6 (54.5%)	4 (57.1%)		
ACS	121 (14.7%)	5 (45.5%)	3 (42.9%)		
Premature discontinuation of DAPT	7 (0.9%)	4 (36.4%)	4 (57.1%)	0.001	0.001
Implanted stent count				0.875	0.926
1	579 (70.4%)	8 (72.7%)	5 (71.4%)		
2	196 (23.8%)	3 (27.3%)	2 (28.6%)		
3	39 (4.7%)	-	-		
4	8 (1%)	-	-		

ACS, acute coronary syndrome; CABG, coronary artery bypass graft; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DAPT, dual antiplatelet therapy; PCI, percutaneous coronary intervention.
*P value between alive and all cause death.
†P value between alive and cardiac death.

Figure 2. Kaplan-Meier estimated survival analysis for all-cause mortality in terms of premature discontinuation of dual antiplatelet therapy.

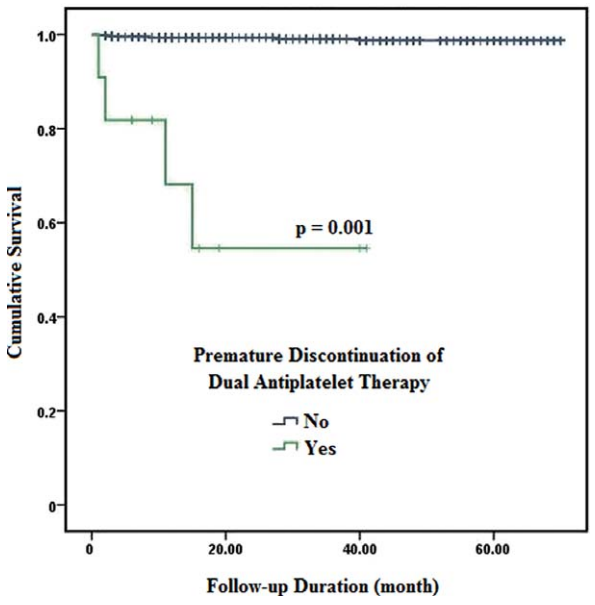
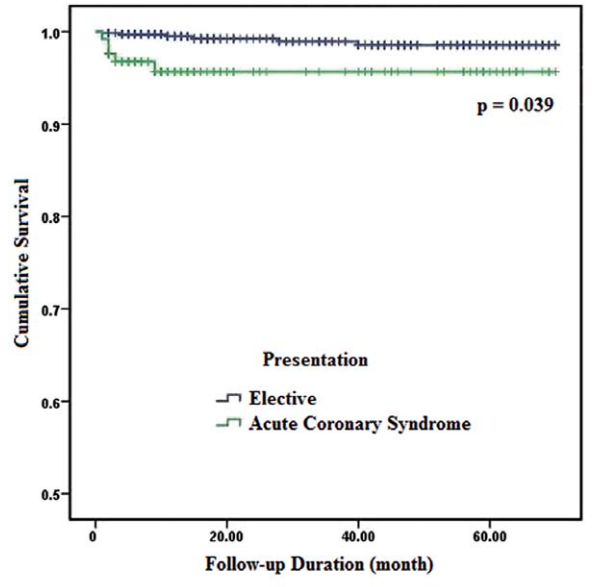
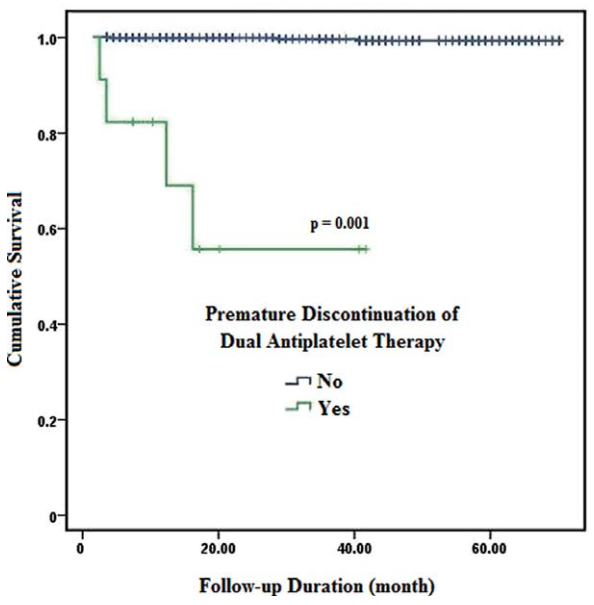


Figure 3. Kaplan-Meier estimated survival analysis for all-cause mortality in terms of clinical presentation of the patients.



compared with those survived (PAD: 28.6% vs. 5.1%, $P = .006$; CVD: 28.6% vs. 2.8%; $P = .001$). Similar to all-cause mortality, the presence of CKD and admission symptoms were significantly different between patient groups. CKD was seen in 14.3% of the patients who deceased of cardiac causes and in 2.4% of patients who survived ($P = .047$). Of the patients who deceased, 45.5% were admitted to the hospital with clinical manifestations of ACS ($P = .038$), while the figure was only 14.7% of those who survived. Premature discontinuation of DAPT was markedly higher in patients who deceased of cardiac causes (57.1% vs. 0.9%; $P = .001$).

Figure 4. Kaplan-Meier estimated survival analysis for cardiac mortality in terms of premature discontinuation of dual antiplatelet therapy.



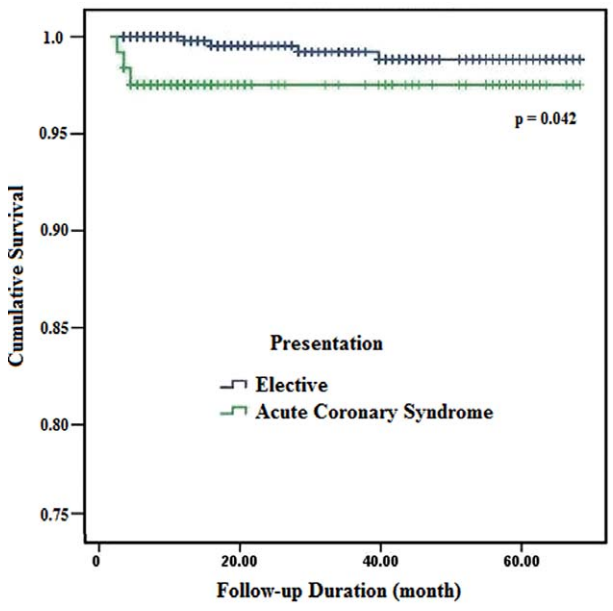
In multivariate analysis of risk factors with a significant affect on cardiac mortality as determined in univariate Cox regression analysis, age (95% CI, 1.104-1.631; $P = .003$), premature discontinuation of DAPT (95% CI, 27.409-13391.68; $P = .001$) (Figure 4), and ACS at admission (95% CI, 1.145-1270.092; $P = .042$) (Figure 5) were found to be predictors of cardiac mortality.

DISCUSSION

Effectiveness and reliability of EES were analyzed in the context of prevalence of seven endpoints, risk factors and predictors of all-cause and cardiac mortality, and multiple clinical and angiographic variables. This study included relatively large number of patients and applied only a few exclusion criteria. Patients and lesions with of varied characteristics were evaluated, providing us with a real-life information.

As an outcome, this real-life stent implantation study has revealed that EES is clinically effective and reliable in the treatment of wide spectrum of coronary artery lesions. During the median 16-month follow-up period, incidence rate of primary endpoints of all-cause mortality and TLF was found to be 1.3% and 2.2%, respectively. Incidence of secondary endpoints of stent thrombosis, TLR, TVR, and MI was 0.24%, 0.8%, 2.2%, and 0.6%, respectively. At this point, it is important to remember

Figure 5. Kaplan-Meier estimated survival analysis for cardiac mortality in terms of clinical presentation of the patients.



that study population had relatively large number of patients with extremely heterogeneous distribution. It included patients with high-risk profile and did not impose strict exclusion criteria. EES implantation proved to be highly effective procedure with a relatively low incidence of adverse events.

Everolimus eluting stents have been subject of multiple studies, including large-scale clinical studies such as A Clinical Evaluation of the XIENCE V and Everolimus Eluting Coronary Stent System in the Treatment of Patients with De Novo Native Coronary Artery Lesions (SPIRIT) II study. EESs have been compared with paclitaxel-eluting stents (PESs) and evaluated separately in studies. SPIRIT II study's 5-year outcomes were published in 2013,[8] SPIRIT III study's 1- and 5-year outcomes were released in 2008 and 2013, respectively,[9,10] and SPIRIT IV 2-year outcomes were published in 2011.[11] Strict clinical and angiographic restrictions were implemented in all three comparisons of EESs and PESs, and the implantation of at most two stents per patient was permitted. In addition to patients with unstable angina pectoris, cases with acute MI, CVD, and CKD (serum creatinine level >2.5 mg/dL or those in need of dialysis) were excluded. Similarly, in the EXecutive RCT: evaluating XIENCE V in a multi-vessel disease (EXECUTIVE) trial (2013), which also compared EESs and PESs, patients who experienced MI within 72 hours and those with the history of CKD or CVD were excluded from the study.[12]

Patients with ostial, bifurcation, left main coronary artery (LMCA), and totally occlusive lesions were not included in SPIRIT studies. Stent diameter was 2.5-4.25 mm in SPIRIT II and 2.5-3.75 mm for SPIRIT III and IV studies. In EXECUTIVE study, patients with LMCA and saphenous vein graft lesions were excluded, and the effectiveness of EES was tested in patients with multiple (2 or 3) vessel disease, including bifurcation lesions. In our study, dimension of the stents was not restricted, and EESs of six diameters (2.25-4.0 mm) and eight lengths (8-38 mm) were implanted. The present study used 33- and 38-mm stents, which were not used in aforementioned studies, in 5.6% (n = 63) of lesions.

Several other large-scale comparative clinical studies on other DESs have been conducted.[13] Furthermore, clinical studies that include test of effectiveness, reliability, and safety of EESs are available.[14] Almost every year, new clinical studies are being conducted on EESs and DESs.[15] Retrospective study of Hermiller et al.[16] and prospective study of Latib et al.[17] were designed as single arm (only EES) trials. The SPIRIT V study tried to overcome restrictions in patient selection implemented in previous SPIRIT studies. Diabetic patients were included, and when needed, more than 1 stent was used for individual patient. Lesions were classified and recorded based on the American College of Cardiology/American Heart Association (ACC/AHA) criteria.[18] Number of lesions and stents were not restricted, and a high-risk group was evaluated separately from low-risk group. Similar to XIENCE V USA,[19] RESOLUTE III All Comers,[20] A Trial of Everolimus-Eluting Stents and Paclitaxel-Eluting Stents for Coronary Revascularization in Daily Practice,[4] and Xience Stent Evaluated at Rotterdam Cardiology Hospital[21] studies, in our study, high-risk patients and lesions were analyzed in the context of whole population.

Inclusion of clinically high-risk patients in DES study is important, as they reflect real-life conditions. In this study, CKD patients constituted 2.6% of total population, and the presence of CKD confronts us as risk factor for all-cause and cardiac mortality. Approach of our center to such patients involves hospitalization of the patient prior to procedure, consultation with nephrology department, cessation of nephrotoxic drugs under the surveillance of health professionals of our service, use of small quantity of contrast material during procedure, and performing procedure on day of dialysis session for dialyzed patients. In the XIENCE V USA study, renal failure, which was detected in nearly 11% of their patients, was found to be predictive factor for stent thrombosis, cardiac mortality, MI, and TLF.

History of CVD is another clinical risk factor. Incidence was 3.0% in total study population. As revealed in many studies, it is strong risk factor for both all-cause and cardiac mortality. The presence of CVD, which was exclusion criterion in SPIRIT study, was found to be a risk factor for cardiac mortality and MI in only XIENCE V USA study. In addition to CVD, another "forgotten" risk factor, PAD, was analyzed in this study and stood out as risk factor for cardiac mortality.

Diabetes mellitus, which is considered to be equivalent to CAD and comes to the forefront as a risk factor at every stage, was detected in 30.7% of present study patients. Though similar incidence of DM was observed in other DES studies, no significant correlation with any endpoint was detected. HT was detected in 62.7% of the patients. Median age of our study population (62.1 years) is comparable to those reported in Photoablation Using the Turbo-Booster and Excimer Laser for In-

Stent Restenosis Treatment (PATENT), and PATENT-2 studies, which investigated the prevalence of HT in Turkish population, concluded in 2005 and 2012, respectively. In both of these studies, the prevalence of HT among individuals aged between 60 and 69 years was 70.0% and 67.9%, respectively.[22,23]

DESs decrease in-stent restenosis by inhibiting neointimal proliferation with anti-proliferative agents they contain. On the other hand, DESs increase risk of thrombosis by delaying endothelization. Therefore, for all DESs, DAPT has vital importance.[24,25] In our study, patient compliance with DAPT was extremely high. The importance of DAPT is emphasized by both physicians and nurses during hospital stay, at discharge, and every polyclinic visit at our center. Results of this study determined premature withdrawal from DAPT to be independent risk factor for all-cause and cardiac mortality. Kaplan–Meier curve of correlation between these endpoints and premature withdrawal from DAPT demonstrated that most of these cases occurred within first few years of follow-up.

CAD is the most common cause of death among men and women. Though in risk scoring for atherosclerosis and clinical cardiovascular disease, male gender is a predominant risk factor, advanced-age female patients are exposed to risks of cardiovascular disease and death as frequently as male patients, if not more. Even though female patients constituted one-quarter of study patient population, half of all-cause and cardiac mortality rates were encountered among female patients. At first glance, it seems to be a contradictory condition, but several studies have yielded comparable results.[26,27] In our study, strong risk factors for CAD, such as DM and HT, were most common among female patients as in other studies.[28] However, female patients were significantly older than male patients. As expected, history of smoking and CAD were most common among men. Higher incidence of CAD among men and increased cardiovascular mortality rate among women are still debatable. Is female gender a risk factor by itself? Or does advanced age in group of female patients and more frequently seen HT and DM among them affect endpoints? A study conducted by Lansky et al.[27] followed-up EESs implanted in 469 male and 200 female patients for 1 year. Although no difference between groups was found regarding all-cause and cardiac mortality rates, LVR and TLR were more frequently seen among female patients.[27] In their study, female patients were relatively older, and DM and HT were most frequently observed. Also, in the XIENCE V USA study, female gender was found in multivariate analysis to be a stronger predictor for cardiac mortality, MI, and TLF. In our study, female gender was also demonstrated to be a risk factor for all-cause and cardiac mortality.

Study Limitations

Despite relatively large number of patients included in our study, this is a single-centered, retrospective study. Median follow-up period was relatively short for the evaluation of stent effectiveness and safety. Due to its design, only Xience V EES was evaluated, and comparative evaluation with other stent types or control group was not performed. Use of or withdrawal from DAPT was determined based on patient's personal statement, which might not reflect real data. Since endpoints were seen in small number of cases, extreme care should be used in the interpretation of risk and predictive factors of statistical analysis.

Dimensions and severity of lesion were not determined using quantitative measurements, but assessments were made based on observational decision of the principal investigator. Many characteristics of lesion, including calcification, ACC/AHA classification, thrombotic load, exit angle, and plaque morphology, were not studied. Intravascular ultrasound employed to determine both lesion characteristics and effectiveness of stent implantation was not performed in this study. In our center, lesions are not classified and intravascular ultrasound is not used routinely. Therefore, we deemed it unnecessary to use assessments and tests not routinely employed in our clinic for this study.

CONCLUSION

Incidence rates of all endpoints, including all-cause mortality and cardiac mortality, were low in EES implanted patients. For all-cause mortality and cardiac mortality; advanced age, ACS at admission, and premature discontinuation of DAPT were predominant predictive risk factors. EES has utmost effectiveness and reliability in the management of coronary artery stenosis.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Hacettepe University (2013:16969557-1200).

Informed Consent: Informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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