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The Influence of Age on Clinical Outcomes in Patients Treated With the Resolute Zotarolimus-Eluting Stent

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Aims: To evaluate the rate of clinical events and bleeding risk according to age in patients undergoing percutaneous coronary intervention (PCI) with a new-generation drug-eluting stent (DES) enrolled in the RESOLUTE Global Clinical Program. Methods: This study represents a pooled analysis of five trials included in the RESOLUTE program including 5,130 patients, of whom 1,675 (32.6%) were ≥70 years old (elderly patients). Results: After adjusting for confounders, age ≥70 years was a significant predictor of high mortality at 30 days (0.6 vs. 0.1%, $P = 0.017$) and 2 years (7.2 vs. 2%, $P < 0.001$). No differences were seen with respect to acute myocardial infarction (MI) or target lesion and vessel revascularization rates between young and elderly patients. Bleeding rates were higher in the elderly throughout follow-up. In the elderly, 7 of the 27 (26%) patients with bleeding episodes died, with a median time between bleeding episode to death of 21 days. In the younger population, 1 patient of 17 with a bleeding episode died (400 days later). Conclusions: Elderly patients undergoing PCI with a new-generation DES have increased mortality and bleeding risk, with similar rates of acute MI and repeat revascularization. Bleeding risk was higher in the elderly and strongly related to death. Target lesion failure rates were not significantly different between the two age groups, suggesting that the Resolute zotarolimus-eluting stent (R-ZES) is effective for patients younger and older than 70 years of age. R-ZES may be recommended for elderly patients when PCI with a DES is identified as a suitable option.

Key words: drug-eluting stents; aged; hemorrhage; myocardial infarction; percutaneous coronary intervention

INTRODUCTION

Cardiovascular disease is currently estimated to affect 82 million American adults, of whom approximately half (40 million) are over 60 years of age [1]. The prevalence is projected to increase significantly over the next two decades. An estimated 8 million additional patients are expected to be diagnosed with coronary heart disease during this time frame [2]. The

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The work represented in this analysis was conducted at multiple sites, the details of which can be obtained in the references.

Conflict of interest: Dr. Belardi has served as a consultant and speaker for Medtronic and Eli Lilly. Dr. Manoharan has served as a consultant to Medtronic. Dr. Widimský has received occasional speaking honoraria from Medtronic. Dr. Silber has received grant, travel, and analysis support from Medtronic for the RESOLUTE All Comers trial. Drs. Albertal, Neumann, Leon, and Saito have no interests to declare.

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elderly have a higher prevalence of all cardiovascular disease compared to younger patients, and significant growth in the elderly population is expected [2]. Thus, specific focus is needed on the treatment of cardiovascular disease in this population.

Elderly patients are often undertreated with evidence based therapies [3–5]. This practice could be due in part to physicians being less confident in the safety and efficacy of therapeutic interventions in the elderly population since they are often underrepresented in clinical trials [6]. Therefore, it is highly important to assess the safety of cardiovascular interventions in these patients.

Drug-eluting stents (DESs) are recommended as a useful alternative to bare metal stents (BMSs) in patients at elevated risk of restenosis who can tolerate and comply with prolonged dual antiplatelet therapy (DAPT) [7].[7] The mean age of patients enrolled in trials of the Resolute zotarolimus-eluting stent (R-ZES; Medtronic) ranged from 60 to 64 years. From a clinical perspective, physicians may be concerned that elderly patients may have different safety and efficacy responses to DES because of complex coronary anatomy or decreased tolerance of (or adherence to) chronic DAPT. The purpose of this analysis is to evaluate the rate of clinical events and bleeding risk in patients $\geq$70 years vs. $<$70 enrolled in the RESOLUTE program.

MATERIALS AND METHODS

Population

The details of the five trials included in the RESOLUTE study program are shown in Table I [8–14]. Uniform end point definitions, adjudication processes, and follow-up procedures were used in all trials.

For the purpose of this analysis, the accrued data from these trials were pooled [8–14]. A cut point of 70 years and above was used to define the elderly population. Comparisons between age categories were made after propensity score adjustment for differences in patient clinical and angiographic characteristics.

Definitions and End points

Demographics and baseline characteristics were summarized by age group ($\geq$70 years and $<$70 years). Clinical outcomes were analyzed, including all-cause death, cardiac death, target vessel myocardial infarction (TVMI), all myocardial infarction (MI), cardiac death or MI, stroke, significant bleeding, stent thrombosis, clinically driven target lesion revascularization (TLR), clinically driven target vessel revascularization (TVR), target lesion failure (TLF), target vessel failure (TVF), and major adverse cardiovascular events (MACEs). TLF was defined as cardiac death, TVMI, or clinically driven TLR. TVF was defined as cardiac death, TVMI, or clinically driven TVR. MACE was defined as all-cause death, MI, emergency coronary artery bypass graft (CABG) surgery, or repeat TLR (clinically driven/clinically indicated) by percutaneous or surgical methods. Stent thrombosis was defined by the Academic Research Consortium (ARC) uniform and hierarchical classification system.

Statistical Analysis

Descriptive statistics were calculated for demographic data, medical history, and clinical characteristics. Between-group comparisons in baseline characteristics were made using Fisher's exact tests for binary variables, Cochran–Mantel–Haenszel tests with modified ridit scores for categorical variables with more than two categories, and *T* tests for continuous variables.

Kaplan–Meier estimates of the cumulative incidence of outcomes were calculated with two-sided 95% confidence intervals for each age group. For each end point, the log-rank test was used for comparison between the two age groups. To adjust for patient characteristics between age groups, propensity scores were calculated using logistic regression with age group ($\geq$70 vs. $<$70 years) as the outcome and the covariates as the predictors. The baseline characteristics included in the propensity score models are shown in the Appendix. Missing data in covariates were imputed with simple imputation before creating the propensity score. Patients were then placed into nonspecific quintiles according to their propensity score [15]. The incidence of each end point was reported by age group. Unadjusted *P* values for the differences in clinical outcomes between age groups were calculated using Fisher's exact test; in addition, the propensity score-adjusted *P* values were provided. All statistical analyses were performed by Harvard Clinical Research Institute using SAS version 9.1 (SAS Institute).

A multiple logistic regression model with variables chosen by a stepwise procedure was used to identify predictors of cardiac death to 2 years. The entry criterion was 0.2, and the stay criterion was 0.1. The following variables were considered in the model: age (years), prior CABG, diabetes mellitus, $\geq 45^{\circ}$ bend, previous MI, preprocedure diameter stenosis (%), unstable angina, hypertension, hyperlipidemia, male gender, degree of calcification, prior percutaneous coronary intervention (PCI), left anterior descending (LAD) lesion, in-stent restenosis (ISR), preprocedure reference vessel diameter (RVD; per mm), TIMI flow 3, current smoker, lesion length (per mm), serum creatinine, and lesion class B2/C.

TABLE I. RESOLUTE Study Program

Study	Design	Eligibility criteria	Primary end point	*n*	Mean age, years	Planned duration of DAPT	Follow-up completed
RESOLUTE First-in-Human Trial[8,9]	Prospective, multicenter, nonrandomized, single-arm, observational study of the R-ZES	Symptomatic ischemic heart disease due to de novo stenotic lesions (>50%) in native coronary arteries; single target lesion with RVD ≥2.5 to ≤3.5 mm, lesion length ≥14 to ≤27 mm, and TIMI flow grade ≥2. Excluded patients with MI <72 hours, prior stent within 30 days, left main or ostial target lesions, severe calcification, bifurcation lesion, target lesion at 45° bend, proximal or distal stenosis >50%, side branch involvement <2.0 mm, LVEF <30%	In-stent late lumen loss at 9 months	139	60.7 ± 10	≥6 months	5 years (97.8%)
RESOLUTE International Trial[10]	Prospective, multicenter, observational registry of the R-ZES	Patients intended to receive ≥1 R-ZES; no restrictions for clinical indication, number of treated vessels/lesions, lesion type, or lesion length	Composite of cardiac death and TVMI at 1 year	2,349	63.5 ± 11.2	≥6 months	3 years (97.2%)
RESOLUTE All Comers Trial[11,12]	Randomized to R-ZES or everolimus-eluting stent. Steering, clinical events, and data management committees, academic research organization, and sponsor were blinded to treatment assignment	Chronic, stable coronary disease or ACS, including non-STEMI, with ≥1 coronary lesion with >50% stenosis in a vessel with reference diameter 2.25–4 mm	TLF (defined as cardiac death, TVMI, or clinically indicated TLR) at 12 months	2,292 ($n = 1,140$ R-ZES; $n = 1,152$ everolimus-eluting stent)	64.4 ± 10.9	≥6 months	4 years (98.4%)
RESOLUTE US Trial[13,14]	Prospective, multicenter, observational study of the R-ZES	Clinical evidence of ischemic heart disease, stable or unstable angina, and/or positive functional study, de novo target lesion(s) of ≥50% stenosis in native coronary artery(ies), TIMI flow ≥2	TLF (defined as cardiac death, TVMI, or clinically indicated TLR) at 12 months (for main cohort)	1,402	64.1 ± 10.7	≥6 months	2 years (main cohort: 96.7%)
RESOLUTE Japan	Prospective, multicenter, observational study of the R-ZES	1 or 2 de novo lesions in native coronary arteries; RVD 2.25–3.5 mm	NA	100	67.7 ± 10.4	≥6 months	3 years (99%)

ACS, acute coronary syndromes; MI, myocardial infarction; NA, not applicable; R-ZES, Resolute zotarolimus-eluting stent; RVD, reference vessel diameter; STEMI, ST-segment elevation myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVMI, target vessel myocardial infarction.

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RESULTS

The pooled cohort consisted of 5,130 patients ($n = 1{,}675$ ≥70 years and $n = 3{,}455$ <70 years). Mean age was 63.8 ± 11.0 years. A greater proportion of elderly patients had diabetes, hypertension, prior PCI, prior CABG surgery, renal impairment, left main involvement, moderate to severe coronary calcification, and measures of complex coronary anatomy compared to patients <70 years (Table II).

Clinical Outcomes

After propensity score adjustment, all-cause and cardiac death was significantly higher among patients ≥70 years compared to patients <70 years at all follow-up time points (Tables III and IV). The cumulative incidence of all-cause death from baseline to 2 years was 7.25% in patients ≥70 years and 1.98% in patients <70 years (log-rank $P < 0.001$; Fig. 1). Analysis of the composite of cardiac death or TVMI revealed similar results (7.2 vs. 4.49%, log-rank $P < 0.001$; Fig. 2). No statistically significant differences between age groups were observed in other individual end points (TVMI, all MI, TLR, or TVR) or in composite end points (cardiac death or TVMI, TLF, TVF, or MACE; Tables III and IV).

Safety Outcomes

Significant bleeding complications were higher among patients ≥70 years of age compared with those <70 years of age throughout follow-up (Tables III and IV, Fig. 3). Of note, bleeding episodes were observed in 27 patients in the elderly group, in whom 7 (26%) died afterward. The median time lapse between a bleeding episode and death was 21 days. Three of the seven bleeding-related deaths occurred during the first 30 days (days 0, 2, and 15), while two deaths occurred very late (days 422 and 701). In this patient subgroup, bleeding-related death accounted for 10% (7/68) of all deaths. On the other hand, 17 bleeding episodes occurred in the younger group. One patient died 400 days after a bleeding event. Atrial fibrillation was not collected as a baseline characteristic but was recorded as an adverse event in all studies except RESOLUTE International. Atrial fibrillation occurred as an adverse event in 1% (9/917) of elderly and 1% (17/1,864) of younger patients; as a severe adverse event, it occurred in, respectively, 3% (25/917) and 1% (20/1,864). Anticoagulation medication for atrial fibrillation was not consistently documented.

The risk of stroke was also higher in the elderly, but only at the 1- and 2-year follow-up time points. Elderly patients had a lower rate of DAPT use than patients <70 years of age at 30 days, 6, and 12 months (Table V). Detailed data relevant to bleeding events (e.g., use of DAPT, concomitant use of warfarin) were not available in an analyzable format.

The risk of stent thrombosis (ARC definite/probable/possible or ARC definite/probable) did not differ by age through 1 year of follow-up. Elderly patients had a slightly higher risk of ARC definite, probable, or possible stent thrombosis through 2 years of follow-up, but no difference was found when the definition was limited to definite or probable stent thrombosis (Tables III and IV; Fig. 4).

Predictors of All-Cause and Cardiac Death

The multivariate model identified several factors that predicted all-cause death at 2 years, including age, serum creatinine, previous MI, diabetes, current smoking, preprocedure diameter stenosis, and TIMI flow 3 (Table VI). In addition to these predictors, prior CABG also predicted cardiac death at 2 years (Table VII).

DISCUSSION

In the present analysis, elderly patients undergoing PCI with a newer-generation DES had an increased risk of adjusted all-cause and cardiac death throughout the entire 2 years of follow-up when compared to the younger population. Accordingly, multivariate logistic analysis showed increasing age as an independent predictor of all-cause and cardiac death. The heightened mortality risk with age observed in the present analysis could be explained by a higher prevalence of comorbidities (i.e., diabetes mellitus, renal failure, previous MI). Additionally, several physiological changes occur with age in (a) homeostasis (i.e., elevated levels of coagulation factors, platelet hyperactivity, enhanced fibrinolysis, and increased blood viscosity), (b) drug metabolism (i.e., reduced hepatic metabolism and renal clearance, altered volume distribution, and changes in protein binding), and (c) hemodynamics (i.e., reduced arterial compliance, increased afterload, ventricular hypertrophy, and reduced coronary perfusion). These alterations observed with aging also influence mortality hazard in the setting of PCI.

With respect to coronary revascularization, stenting is usually challenging in elderly patients due to a higher prevalence of multivessel disease and increased lesion calcification and tortuosity. Of note, mortality risk in the elderly patients we analyzed was not driven by an excess risk of stent thrombosis or reintervention. This result confirms the safety and overall performance of this new-generation DES in this patient population despite an elevated risk profile. On the other hand, as

TABLE II. Baseline Patient and Lesion Characteristics

Characteristics	Age ≥ 70 years ($n = 1,675$)	Age < 70 years ($n = 3,455$)	P value
Age, mean ± SD (years)	76 ± 4.6	58 ± 7.9	<0.001
Men	66.9% (1,120)	78.8 (2,722)	<0.001
Diabetes mellitus	34.3% (574)	27.8% (961)	<0.001
Insulin-dependent	9.8% (164)	8.4% (291)	0.116
Hypertension	80.3% (1,345)	70.0% (2,418)	<0.001
Hyperlipidemia	72.1% (1,207)	71.3% (2,463)	0.575
Prior MI	26.4% (437)	26.5% (908)	0.946
History of smoking	45.6% (764)	65.4% (2,261)	<0.001
Prior PCI	33.6% (562)	29.6% (1,023)	0.005
Prior CABG	13.1% (220)	6.3% (219)	<0.001
BMI, mean ± SD (kg/m^2)	27.8 ± 4.6	28.9 ± 5.3	<0.001
Reason for revascularization			0.002
Stable angina	38.1% (639)	38.7% (1,337)	
Unstable angina	27.1% (454)	25.3% (875)	
Myocardial infarction	19.7% (330)	23.8% (823)	
Silent ischemia	3.5% (59)	3.0% (102)	
Acute coronary syndrome	42.7% (489/1,144)	48.7% (1,143/2,345)	<0.001
AMI within 72 hr	12.4% (207)	17.1% (592)	<0.001
LVEF			0.374
<30%	2.3% (27/1,170)	1.8% (42/2,341)	
30–40%	9.1% (106/1,170)	8.2% (191/2,341)	
>40%	88.6% (1,037/1,170)	90.0% (2,108/2,341)	
Serum creatinine, mean ± SD (μmol/L)	94.4 ± 39.2 (1,510)	85.2 ± 36.1 (3,092)	<0.001
Creatinine clearance			
Mean ± SD (mL/min)	68.26 ± 25.17	105.1 ± 34.76	<0.001
<60 mL/min	39.3% (593/1,510)	5.8 (179/3,092)	<0.001
Multivessel stenting	15.7% (263)	14.7% (507)	0.338
Vessel location			
LAD	48.4% (810)	50.0% (1,726)	0.284
LCX	30.7% (514)	29.6% (1,022)	0.417
RCA	33.3% (557)	33.6% (1,161)	0.825
LMCA	2.9% (48)	1.4% (47)	<0.001
SVG	1.9% (32)	0.9% (32)	0.004
Lesion class B2/C	67.5% (1,492/2,208)	66.6% (2,922/4,389)	0.422
Moderate/severe calcification	41.3% (906/2,193)	27.3% (1,193/4,367)	<0.001
Tortuosity (bend ≥ 45°)	23.3% (502)	19.6% (832)	0.003
TIMI flow 3	82.8% (1,828/2,208)	76.8% (3,371/4,388)	<0.001
RVD, mean ± SD (mm)	2.76 ± 0.51 (2,134)	2.79 ± 0.51 (4,186)	0.008
RVD < 2.5 mm	32.5% (528/1,624)	29.2% (971/3,328)	0.018
RVD 2.5–3.5 mm	69.7% (1,132/1,624)	73.1% (2,334/3,328)	0.013
RVD > 3.5 mm	7.1% (115/1,624)	7.0% (232/3,328)	0.906
Minimal lumen diameter, mean ± SD (mm)	0.69 ± 0.46 (2,197)	0.66 ± 0.46 (4,372)	0.004
Diameter stenosis, mean ± SD (%)	74.52 ± 16.31 (2,197)	76.04 ± 16.42 (4,372)	<0.001
Lesion length, mean ± SD (mm)	15.23 ± 8.82 (2,130)	15.98 ± 9.73 (4,165)	0.002
Lesion length > 27 mm	10.7% (173)	11.4% (379)	0.442
Lesion length > 18 mm	30.7% (498)	33.7% (1,116)	0.039
Small vessel ≤ 2.75 mm	60.1% (976)	54.3% (1,806)	<0.001
Bifurcation	14.7% (246)	14.8% (510)	0.967
Total occlusion	7.2% (120)	11.2% (387)	<0.001
ISR	6.1% (102)	5.2% (180)	0.214
Number of stents per patient, mean ± SD	1.53 ± 0.98	1.50 ± 0.89	0.187
Postdilatation	42.4% (711)	44.2% (1,527)	0.242
Length of stay, mean ± SD (days)	2.28 ± 3.24	1.98 ± 2.54	0.001

AMI, acute myocardial infarction; BMI, body mass index; CABG, coronary artery bypass graft; ISR, in-stent restenosis; LAD, left anterior descending; LCX, left circumflex; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery; RVD, reference vessel diameter; SD, standard deviation; SVG, saphenous vein graft.

the elderly population had a higher mortality rate, it is possible that reintervention was underestimated by competing risks. Nevertheless, recent studies have demonstrated the superiority of DES over BMS in this specific patient subset [16,17]. Surely, age represents a clinically relevant factor to take into account during

TABLE III. Clinical Outcomes According to Age: In-Hospital and 30-Day Follow-Up

	In-hospital				30-Day			
End point	Age ≥ 70 years ($n = 1,675$)	Age < 70 years ($n = 3,455$)	*P* value	Adjusted *P* value	Age ≥ 70 years ($n = 1,667$)	Age < 70 years ($n = 3,448$)	*P* value	Adjusted *P* value
Death	0.4% (6)	0.1% (2)	0.018	0.041	0.6% (10)	0.1% (4)	0.003	0.017
Cardiac death	0.4% (6)	0.0% (1)	0.006	0.027	0.6% (10)	0.1% (3)	0.001	0.012
TVMI	1.9% (31)	2.3% (81)	0.355	0.169	2.2% (36)	2.6% (88)	0.438	0.272
Q wave	0.1% (1)	0.3% (11)	0.119	0.056	0.2% (4)	0.4% (15)	0.336	0.307
Non-Q wave	1.8% (30)	2.0% (69)	0.744	0.431	1.9% (32)	2.1% (74)	0.676	0.447
Cardiac death or TVMI	2.1% (36)	2.3% (81)	0.764	0.470	2.6% (43)	2.6% (91)	0.926	0.705
All MI	2.3% (38)	2.4% (84)	0.770	0.492	2.2% (37)	2.6% (90)	0.444	0.319
Stroke	0.1% (1/758)	0.1% (2/1,591)	>0.99	0.664	0.5% (4/756)	0.1% (2/1,589)	0.089	0.124
Significant bleeding complications	1.3% (10/758)	0.3% (5/1,591)	0.009	0.018	1.6% (12/756)	0.5% (8/1,589)	0.014	0.031
ARC def/prob/poss stent thrombosis	0.2% (4)	0.4% (13)	0.605	0.433	0.6% (10)	0.6% (20)	>0.99	0.753
ARC def/prob stent thrombosis	0.2% (3)	0.4% (13)	0.294	0.249	0.6% (10)	0.6% (20)	>0.99	0.753
Clinically driven TLR	0.3% (5)	0.4% (15)	0.634	0.729	0.8% (14)	0.7% (23)	0.486	0.357
Clinically driven TVR	0.4% (6)	0.5% (16)	0.657	0.872	1.0% (16)	0.9% (30)	0.753	0.634
TLF[a]	2.4% (41)	2.5% (88)	0.924	0.766	3.1% (52)	2.9% (101)	0.726	0.751
TVF[b]	2.5% (42)	2.5% (88)	>0.99	0.838	3.2% (54)	3.1% (106)	0.733	0.861
MACE[c]	2.5% (42)	2.6% (90)	0.925	0.834	3.2% (53)	3.0% (104)	0.795	0.728

ARC, Academic Research Consortium; MACE, major adverse cardiac events; MI, myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVF, target vessel failure; TVMI, target vessel myocardial infarction; TVR, target vessel revascularization.

[a]Cardiac death, TVMI, or clinically driven TLR.

[b]Cardiac death, TVMI, or clinically driven TVR.

[c]Defined as all-cause death, MI, emergency coronary artery bypass surgery, or repeat TLR (clinically driven/clinically indicated) by percutaneous or surgical methods.

clinical decision-making; however, it should not contraindicate the revascularization procedure.

Over half of the deaths were due to cardiac causes and therefore may have been amenable to interventions or therapies that reduce the risk of subsequent cardiovascular events. While bleeding complications could be inconsequential in younger patients, they are usually not well tolerated by elderly patients and could lead to ischemic cardiovascular events [18–21]. In the present study, 10% of the deaths observed in the elderly were closely related to a bleeding episode, but this complication did not lead to death in the younger individuals. Cessation of evidence-based medicines, negative effect of transfusions, and the reduction of oxygen delivery due to the bleeding itself are most likely contributors to the inherent ischemic risk of bleeding. In contemporary PCI, several measures can be implemented to reduce bleeding rates, such as the use of radial access, administration of bivalirudin, and reduction of aspirin dose or avoidance of potent antiplatelets in patients with high bleeding risk.

In the present study, the risk of very late stent thrombosis (between 1 and 2 years) was higher in elderly vs. younger patients when possible events were counted. The potential contribution of DAPT cessation due to bleeding to the risk of stent thrombosis warrants consideration and further research. Furthermore, hesitation to prescribe DAPT because of bleeding risk concerns constitutes a barrier to DES use in the elderly population. Currently recommended DAPT regimens may not be optimally dosed for the elderly since the elderly were underrepresented by the trials that established these regimens [22]. More research is needed to determine the optimal antithrombotic regimen in elderly patients to prevent both stent thrombosis and bleeding complications.

This analysis has several limitations. We did not compare R-ZES vs. BMS in this analysis and therefore cannot assess the influence of R-ZES on clinical outcomes in this population. As noted before, there is considerable data supporting the use of DES in this particular age group. This analysis was a comparison according to an arbitrary age cutoff point. The analyzed data were pooled across several different studies with different designs but consistent definitions and end points. Data on atrial fibrillation–related anticoagulant medication were not collected uniformly, and non-DAPT concomitant medications were not collected in RESOLUTE International and RESOLUTE Japan. As a result, the available data for our analysis do not allow

TABLE IV. Clinical Outcomes According to Age: 1- and 2-Year Follow-Up

	1 year				2 years			
End point	Age ≥ 70 years ($n = 1,660$)	Age < 70 years ($n = 3,429$)	P value	Adjusted P value	Age ≥ 70 years ($n = 1,643$)	Age < 70 years ($n = 3,371$)	P value	Adjusted P value
Death	3.9% (64)	0.9% (32)	<0.001	<0.001	7.2% (118)	2.0% (67)	<0.001	<0.001
Cardiac death	2.3% (38)	0.6% (20)	<0.001	<0.001	4.4% (72)	1.2% (40)	<0.001	<0.001
TVMI	2.7% (45)	3.0% (104)	0.595	0.266	3.4% (56)	3.5% (117)	0.935	0.429
Q wave	0.3% (5)	0.5% (18)	0.373	0.162	0.4% (7)	0.7% (24)	0.255	0.086
Non-Q wave	2.4% (40)	2.5% (87)	0.848	0.553	3.0% (49)	2.8% (94)	0.718	0.958
Cardiac death or TVMI	4.6% (77)	3.5% (121)	0.063	0.204	7.1% (117)	4.5% (153)	<0.001	0.004
All MI	3.1% (51)	3.2% (111)	0.799	0.491	3.8% (63)	3.9% (131)	1.000	0.521
Stroke	1.6% (12/753)	0.3% (5/1,581)	0.001	0.020	2.6% (19/743)	0.7% (11/1,553)	<0.001	0.005
Significant bleeding complications	2.9% (22/753)	0.9% (15/1,581)	<0.001	0.001	3.6% (27/743)	1.1% (17/1,553)	<0.001	<0.001
ARC def/prob/poss stent thrombosis	1.7% (29)	1.1% (39)	0.090	0.145	3.3% (54)	1.8% (60)	0.001	0.013
Early (≤30 days)	0.6% (10)	0.6% (20)	>0.99	0.757	0.6 (10)	0.6% (20)	1.000	0.734
Late (>30 and ≤360 days)	1.2% (20)	0.6% (20)	0.026	0.074	1.2% (20)	0.6% (20)	0.027	0.075
Very late (>360 days)					1.5% (25)	0.6% (21)	0.003	0.034
ARC def/prob stent thrombosis	0.7% (12)	0.8% (28)	0.866	0.754	0.9% (14)	1.0%	0.756	0.572
Early (≤30 days)	0.6% (10)	0.6% (20)	>0.99	0.729	0.6% (10)	0.6% (20)	1.000	0.734
Late (>30 and ≤360 days)	0.1% (2)	0.3% (9)	0.521	0.130	0.1% (2)	0.3% (9)	0.521	0.131
Very late (>360 days)					0.1% (2)	0.1% (5)	1.000	0.442
Clinically driven TLR	3.3% (54)	3.2% (111)	>0.99	0.729	4.4% (72)	4.9% (165)	0.436	0.299
Clinically driven TVR	4.5% (75)	4.2% (144)	0.606	0.789	6.5% (106)	6.8% (228)	0.717	0.266
TLF[a]	7.4% (123)	6.2% (211)	0.091	0.349	10.8% (177)	8.5% (288)	0.013	0.061
TVF[b]	8.7% (144)	6.9% (236)	0.026	0.208	12.7% (208)	10.1% (339)	0.006	0.079
MACE[c]	9.2% (153)	6.7% (229)	0.001	0.018	13.8% (227)	9.7% (326)	<0.001	<0.001

ARC, Academic Research Consortium; MACE, major adverse cardiac events; MI, myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVF, target vessel failure; TVMI, target vessel myocardial infarction; TVR, target vessel revascularization.

[a]Cardiac death, TVMI, or clinically driven TLR.

[b]Cardiac death, TVMI, or clinically driven TVR.

[c]Defined as all-cause death, MI, emergency coronary artery bypass surgery, or repeat TLR (clinically driven/clinically indicated) by percutaneous or surgical methods.

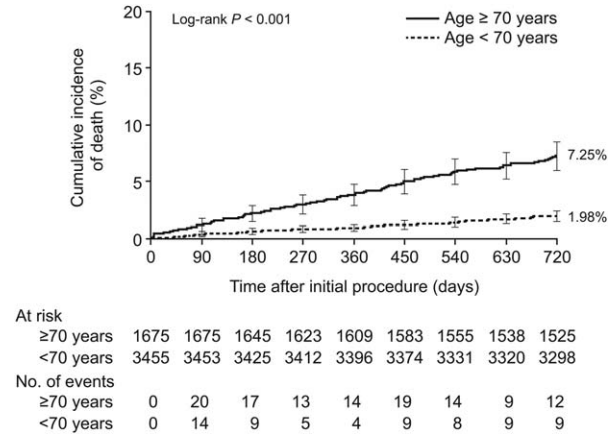

Fig. 1. Cumulative incidence of death through 24 months.

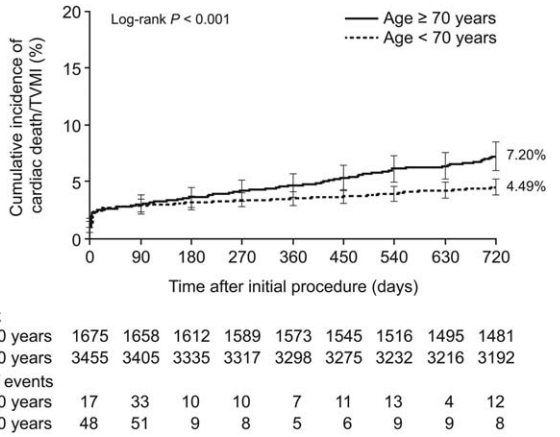

Fig. 2. Cumulative incidence of cardiac death or target vessel myocardial infarction (TVMI) through 24 months.

an investigation into whether such medications led to a clinically significant increase in bleeding risk. Finally, although we adjusted death rates, unmeasured confounders may have been present.

CONCLUSIONS

Elderly patients undergoing PCI were at increased risk of all-cause and cardiac death immediately after stent

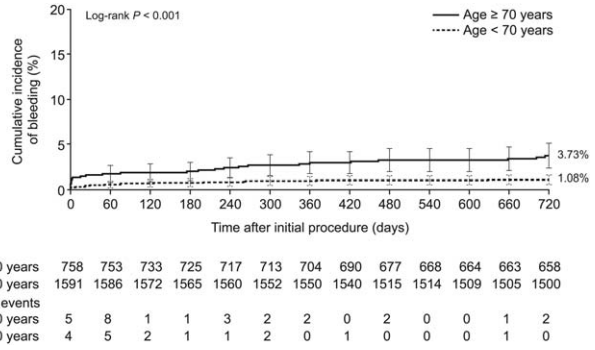

Fig. 3. Cumulative incidence of major bleeding through 24 months.

TABLE V. Dual Antiplatelet Therapy Use[a]

	Age ≥ 70 years	Age < 70 years	*P* value
30 days	95.6%	97.1%	0.006
6 months	93.7%	95.3%	0.020
12 months	87.6%	90.3%	0.004
24 months	45.7%	45.5%	0.877

[a]Dual antiplatelet therapy was aspirin or clopidogrel in most patients. In the ≥70 and <70 year age groups, 0.8 and 1.0% of patients took prasugrel (13/1,675 and 36/3,455), and 0.6 and 0.5% took ticlopidine (10/1,675 and 17/3,455).

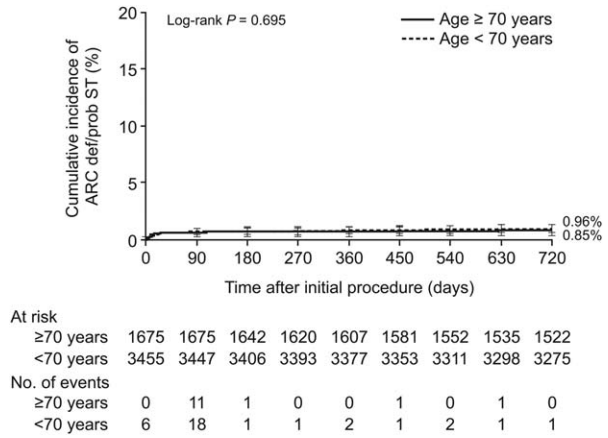

Fig. 4. Cumulative incidence of Academic Research Consortium (ARC) definite or probable stent thrombosis through 24 months.

placement and throughout 2-year follow-up. However, TLF rates were not significantly different between the two age groups, suggesting that the R-ZES is effective for patients younger and older than 70 years of age. The increased mortality hazard was not due to R-ZES-related complications but to the inherent risk of aging and associated comorbidities. In the elderly, bleeding episodes were strongly related to death, suggesting that clinicians should closely monitor these patients and their medication regimens post-PCI in order to consider modifications for early signs of bleeding. More research is needed to evaluate the effect of R-ZES vs. BMS on clinical outcomes in this population; more research is also needed to determine the optimal dose and duration of DAPT to maximize clinical benefits and minimize bleeding risks. R-ZES may be recommended for elderly patients when PCI with a DES is identified as a suitable option.

TABLE VI. Predictors of All-Cause Death at 2 Years

Predictor	Coefficient	Standard error	Odds ratio	*P* value
Intercept	−11.53	0.89	–	<0.001
Age (years)	0.08	0.01	1.087	<0.001
Serum creatinine (μmol/L)	0.01	0.00	1.007	<0.001
Previous MI	0.55	0.16	1.733	<0.001
History of diabetes	0.49	0.16	1.637	0.002
Current smoker	0.56	0.21	1.748	0.008
Preprocedure diameter stenosis (%)	0.02	0.01	1.016	0.008
TIMI flow 3	0.53	0.23	1.705	0.02
History of hyperlipidemia	−0.29	0.17	0.747	0.087

MI, myocardial infarction.

TABLE VII. Predictors of Cardiac Death at 2 Years

Predictor	Coefficient	Standard error	Odds ratio	*P* value
Intercept	−11.54	1.05	–	<0.001
Age (years)	0.09	0.01	1.091	<0.001
Current smoker	0.83	0.25	2.285	0.001
History of diabetes	0.62	0.2	1.867	0.002
Serum creatinine (μmol/L)	0.00	0.00	1.005	0.003
Prior CABG	0.63	0.26	1.878	0.016
Previous MI	0.49	0.21	1.630	0.018
Preprocedure diameter stenosis (%)	0.01	0.01	1.013	0.049
History of hyperlipidemia	−0.39	0.21	0.680	0.072

CABG, coronary artery bypass graft; MI, myocardial infarction.

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