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Coronary Stenting With the Genous™ Bio-Engineered R Stent™ in Elderly Patients

– 12-Month Outcomes From the e-HEALING Registry –

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Background: We evaluated the Genous™ Bio-engineered R stent™ in elderly patients undergoing non-urgent percutaneous coronary intervention. The elderly have an increased risk of (temporary) discontinuation of clopidogrel, which is associated with a higher risk of developing stent thrombosis (ST).

Methods and Results: In the e-HEALING registry, 2,651 patients were <65, 1,403 were 65–74 and 869 were ≥75 years old. The 12-month primary outcome was target vessel failure (TVF), defined as target vessel-related cardiac death or myocardial infarction and target vessel revascularization. Secondary outcomes included target lesion revascularization (TLR) and ST. Cumulative event rates were estimated with the Kaplan-Meier method and compared with a log-rank test. TVF occurred significantly more often in elderly patients compared with younger patients (7.0% in patients aged <65, 8.8% in patients aged 65–74 and 11.7% in patients aged ≥75 years, P<0.001). There was a trend to higher TLR with increasing age (log-rank P=0.06) and no difference in ST.

Conclusions: The 1-year results of the Genous stent in a population of elderly patients show a significantly higher TVF rate compared with younger patients, mainly driven by a higher mortality. Although there was a trend to higher TLR rates with increasing age, there was no difference in ST. This attests to the safety of this therapy for the elderly, in whom there could be concerns with administering long-term dual antiplatelet therapy. (*Circ J* 2011; **75:** 2590–2597)

Key Words: e-HEALING; Elderly; Genous™ EPC capturing R stent™; 12-month outcomes

As a consequence of the increasing age of populations worldwide, the elderly represent an important subgroup of patients undergoing percutaneous coronary intervention (PCI). These elderly constitute a high-risk group for complications after PCI.[1] Yet despite higher mortality, vascular and bleeding complications; restenosis rates after bare-metal stenting (BMS) have been reported to be comparable to those of younger patients.[2] Compared with BMS, drug-eluting stents (DES) have been shown to reduce the incidence of in-stent-restenosis by inhibiting or delaying neo-endothelialization.[3–5] In 2 large registries, the use of DES in the elderly was associated with lower repeat revascularization rates when compared with BMS placement.[6,7] However, treating the elderly with DES is potentially hampered by an increased incidence of comorbidities, the increased need for (non-)cardiovascular interventions with the accompanying temporary discontinuation of antiplatelet therapy, and low therapeutic compliance or drug interactions because of multiple medications. Thus the elderly patients are at an increased risk of (temporary) discontinuation of clopidogrel, which is associated with a higher risk of developing stent thrombosis (ST).[8,9] The Genous™ endothelial progenitor cell (EPC) capturing stent™ has been shown to be associated with a low incidence of repeat revascularization and ST at 12 months with the recommended month of dual antiplatelet therapy (DAPT).[10]

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Table 1. Baseline Characteristics of the Study Patients

	<65 years (n=2,651)	65–74 years (n=1,403)	≥75 years (n=869)	P value
Demographics, no./total no. (%)				
Age, median (IQR)	55 (49–60)	69 (67–72)	78 (76–81)	–
Male sex	2,296/2,651 (86.6%)	1,031/1,402 (73.5%)	555/869 (63.9%)	<0.001
BMI, mean (SD)	27.6 (5.0)	27.2 (4.4)	26.5 (4.1)	<0.001
Diabetes				
Any	623/2,651 (23.5%)	402/1,403 (26.7%)	207/869 (23.8%)	0.20
Insulin-requiring	127/2,651 (4.8%)	92/1,403 (6.6%)	53/869 (6.1%)	0.41
Hypertension	1,662/2,647 (62.8%)	1,015/1,401 (72.4%)	685/866 (79.3%)	<0.01
Hypercholesterolemia	2,012/2,647 (76.0%)	1,035/1,395 (74.2%)	609/866 (70.6%)	0.001
Current smoker	892/2,651 (33.6%)	250/1,403 (17.8%)	87/869 (10.0%)	<0.001
Family history of MI	868/2,642 (32.9%)	356/1,401 (25.4%)	152/864 (17.6%)	<0.001
Congestive heart failure	71/2,638 (2.7%)	45/1,396 (3.2%)	60/863 (7.0%)	<0.001
History, no./total no. (%)				
MI	967/2,651 (36.5%)	491/1,403 (35.0%)	355/869 (40.9%)	0.09
PCI	469/2,651 (17.7%)	288/1,403 (20.5%)	185/869 (21.3%)	<0.01
CABG	113/2,651 (4.3%)	123/1,403 (8.8%)	65/869 (7.5%)	<0.001
Prior stroke	113/2,642 (4.3%)	110/1,398 (7.9%)	72/864 (8.3%)	<0.001
Indication for PCI, no./total no. (%)				<0.01
Elective	1,262/2,651 (47.6%)	695/1,403 (49.5%)	321/869 (36.9%)	
ACS	1,148/2,651 (43.3%)	603/1,403 (43.0%)	482/869 (55.5%)	
Other/unknown	241/2,651 (9.1%)	105/1,403 (7.5%)	66/869 (7.6%)	
Medication use, no./total no. (%)				
Aspirin	2,209/2,651 (83.3%)	1,184/1,403 (84.4%)	688/869 (79.2%)	0.03
Clopidogrel	1,643/2,651 (62.0%)	816/1,403 (58.2%)	454/869 (52.2%)	<0.001
ARBs	263/2,651 (9.9%)	152/1,403 (10.8%)	111/869 (12.8%)	0.02
ACEIs	879/2,651 (33.2%)	565/1,403 (40.3%)	364/869 (41.9%)	<0.001
β-blockers	1,460/2,651 (55.1%)	830/1,403 (59.2%)	498/869 (57.3%)	0.08
Calcium antagonists	294/2,651 (11.1%)	270/1,403 (19.2%)	181/869 (20.8%)	<0.001
Nitrates	727/2,651 (27.4%)	495/1,403 (35.3%)	346/869 (39.8%)	<0.001
Statins	2,166/2,651 (81.7%)	1,135/1,403 (80.9%)	644/869 (74.1%)	<0.001

IQR, interquartile range; BMI, body mass index; SD, standard deviation; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; ACS, acute coronary syndrome; ARB, angiotensin II receptor blocker; ACEI, angiotensin-converting-enzyme inhibitor.

In the present study, we investigated the 12-month outcomes, with regard to ischemic events, repeat intervention and ST, of a subgroup of elderly patients treated with the Genous stent during routine non-urgent PCI using data from the multicenter, prospective worldwide e-HEALING registry.

Methods

Study Design

The current analysis is a post-hoc analysis of the e-HEALING registry. The study design, data collection and management, quality control and list of sites/investigators have been published previously.[10] The e-HEALING (Healthy Endothelial Accelerated Lining Inhibits Neointimal Growth) was a worldwide, multicenter post-marketing registry. Approximately 5,000 patients were included between October 2005 and October 2007 from 144 centers in Europe, Asia/Pacific, Middle East, Africa, and Latin America. The local medical ethics committees approved the study protocol at sites at which such approval was required. If determined necessary, the patient's written informed consent was obtained.

Device Description

The Genous stent comprises a polysaccharide matrix coating with monoclonal murine anti-human $CD34^+$ antibodies covalently bonded to a 316L stainless steel stent (Genous™ Bio-engineered R stent™, OrbusNeich Medical Technologies, Fort Lauderdale, FL, USA).

Study Population and Procedures

Patients undergoing non-urgent PCI with at least 1 lesion suitable for stenting with a Genous stent (diameter 2.50–4.00 mm, length 9–33 mm) in accordance with the manufacturer's Instructions for Use were eligible for inclusion in the e-HEALING registry. The indication for PCI was left to the discretion of the operator. Patients were recommended to receive at least 2 weeks of statin therapy prior to PCI, DAPT for at least 1 month post-procedure and aspirin indefinitely. The use of concomitant medication was left to the discretion of each participating center. In cases of multiple lesions, all lesions were preferably treated with a Genous stent but this was not mandatory per protocol.

Elderly Patients

For our current analyses, we formed the following 4 age groups: <65 years, 65–74 years, 75–84 years and ≥85.[11] Elderly patients were defined as aged ≥65 years.

Table 2. Baseline Angiographic and Procedural Characteristics

	<65 years	65–74 years	≥75 years	P value
Patient characteristics	n=2,651	n=1,403	n=869	
Target lesion coronary artery				
Multivessel PCI	420/2,645 (15.9%)	246/1,397 (17.6%)	169/868 (19.5%)	0.01
Bypass graft	14/2,645 (0.5%)	16/1,397 (1.1%)	15/868 (1.7%)	0.01
Left main	36/2,645 (1.4%)	32/1,397 (2.3%)	21/868 (1.9%)	0.02
Lesions per patient, mean (SD)	1.3 (0.6)	1.4 (0.6)	1.4 (0.7)	<0.01
Lesion characteristics	n=3,484	n=1,900	n=1,213	
Lesion type, no./total no. (%)				0.13
De novo	3,412/3,484 (97.9%)	1,854/1,900 (97.6%)	1,179/1,213 (97.2%)	
Restenotic	72/3,484 (2.1%)	46/1,900 (2.4%)	34/1,213 (2.8%)	
Bifurcation lesion	326/3,484 (9.4%)	202/1,900 (10.6%)	137/1,213 (11.3%)	0.03
Lesion classification, no./total no. (%)				<0.001
A	658/3,484 (18.9%)	228/1,900 (12.0%)	120/1,213 (10.1%)	
B1	1,238/3,484 (35.5%)	672/1,900 (35.4%)	426/1,213 (35.8%)	
B2	898/3,484 (25.8%)	650/1,900 (34.2%)	419/1,213 (33.8%)	
C	690/3,484 (19.8%)	350/1,900 (18.4%)	248/1,213 (20.4%)	
Baseline angiographic findings – mean (SD)				
Lesion length, mm	17 (9)	16 (8)	16 (9)	<0.001
Reference vessel diameter, mm	3.0 (0.4)	3.0 (0.4)	3.0 (0.4)	0.43
Stenosis, % of vessel diameter	85 (12)	85 (13)	85 (11)	0.35
Baseline TIMI flow grade, no./total no. (%)				<0.001
0	384/3,484 (11.0%)	164/1,900 (8.6%)	106/1,213 (8.7%)	
1	448/3,484 (12.9%)	151/1,900 (7.9%)	73/1,213 (6.0%)	
2	710/3,484 (20.4%)	298/1,900 (15.7%)	170/1,213 (14.0%)	
3	1,942/3,484 (55.7%)	1,287/1,900 (67.7%)	864/1,213 (72.2%)	
Stent use				
Stents per lesion, mean (SD)	1.1 (0.4)	1.1 (0.5)	1.1 (0.5)	0.86
Type of stent placed				0.31
Genous only	3,006/3,484 (86.3%)	1,596/1,900 (84.0%)	1,030/1,213 (84.9%)	
Genous and/or other	420/3,484 (12.0%)	261/1,900 (13.7%)	152/1,213 (12.5%)	
No or unknown	58/3,484 (1.7%)	43/1,900 (2.3%)	31/1,213 (2.6%)	
Direct stenting attempted	1,395/3,484 (40.0%)	714/1,900 (37.6%)	381/1,213 (31.4%)	<0.001
Final angiographic findings – mean (SD)				
Reference vessel diameter, mm	3.1 (0.4)	3.1 (0.4)	3.0 (0.4)	0.43
Stenosis, % of vessel diameter	5 (17)	4 (11)	3 (9)	<0.001
Final TIMI flow grade, no./total no. (%)				<0.001
0	158/3,484 (4.5%)	37/1,900 (1.9%)	4/1,213 (0.3%)	
1	23/3,484 (0.7%)	11/1,900 (0.6%)	3/1,213 (0.2%)	
2	165/3,484 (4.7%)	29/1,900 (1.5%)	17/1,213 (1.4%)	
3	3,138/3,484 (90.1%)	1,823/1,900 (95.9%)	1,189/1,213 (98.0%)	

TIMI, Thrombolysis In Myocardial Infarction. Other abbreviations see in Table 1.
Angiographic variables were obtained by visual assessment.

Outcomes

The main outcome of the e-HEALING registry was target vessel failure (TVF) at 12-month follow-up, defined as a composite of cardiac death or myocardial infarction (MI) unless unequivocally attributable to a non-target vessel and target vessel revascularization (TVR). Secondary outcomes were a composite of cardiac death, MI, and clinically-indicated target lesion revascularization (TLR), the individual outcomes of all-cause death, cardiac death, MI (non-Q-wave or Q-wave), TLR, TVR, ST according to the definitions of the Academic Research Consortium (ARC),[12] major and minor bleeding, and stroke. A non-Q-wave MI was defined as an elevation of post-procedural creatine kinase (CK) levels greater than 2-fold the upper limit of normal (ULN) in the absence of pathological Q-waves. A Q-wave MI was defined as the development of new, pathological Q-waves in 2 or more contiguous leads with an elevation of CK-MB above the ULN. TLR was defined as any repeat PCI of the target lesion or coronary artery bypass grafting of the target vessel. Revascularization was indicated clinically if the stenosis of the treated lesion was at least 50% of the lumen diameter based on quantitative coronary angiography with 1 of the following: a positive history of recurrent angina pectoris, objective signs of ischemia at rest (ECG changes) or a positive ischemia-detection test, or abnormal results of any invasive functional diagnostic test. Revascularization of a stenosis of at least 70% of the lumen diameter in the absence of the aforementioned ischemic signs or symptoms was also considered a TLR. TVR was defined as repeat revas-

Table 3. 12-Month Outcomes

	<65 years (n=2,651), n (%)**	65–74 years (n=1,403), n (%)**	≥75 years (n=869), n (%)**	P value†
Main composite outcome				
TVF*	178 (7.0%)	120 (8.8%)	97 (11.7%)	<0.001
Individual outcomes				
Death	33 (1.3%)	34 (2.5%)	43 (5.2%)	<0.001
Cardiac death	26 (1.0%)	25 (1.8%)	28 (3.4%)	<0.001
MI	46 (1.8%)	24 (1.7%)	21 (2.5%)	0.37
Q-wave MI	14 (0.5%)	2 (0.2%)	0 (0.0%)	
Non-Q-wave MI	33 (1.3%)	22 (1.6%)	21 (2.2%)	
TLR	126 (5.0%)	80 (6.0%)	57 (7.1%)	0.06
PCI	114 (4.5%)	74 (5.5%)	54 (6.7%)	
CABG	18 (0.7%)	9 (0.7%)	3 (0.4%)	
TVR	143 (5.6%)	90 (6.7%)	66 (8.2%)	0.03
PCI	126 (5.0%)	80 (6.0%)	61 (7.6%)	
CABG	23 (0.9%)	13 (1.0%)	5 (0.6%)	
Composite outcomes				
Device oriented: cardiac death, target vessel MI, TLR	165 (6.4%)	112 (8.2%)	89 (10.8%)	<0.001
Patient oriented: death, MI, any revascularization	260 (10.1%)	174 (12.8%)	134 (16.1%)	<0.001
Cardiac death, MI, TLR	166 (6.5%)	115 (8.5%)	93 (11.3%)	<0.001
Death or MI	73 (2.8%)	56 (4.1%)	59 (7.0%)	<0.001
Cardiac death or MI	66 (2.5%)	47 (3.4%)	46 (5.5%)	<0.001
Other events				
Bleeding	17 (0.6%)	24 (1.7%)	25 (3.0%)	<0.001
Major	6 (0.2%)	11 (0.8%)	9 (1.1%)	
Minor	11 (0.4%)	13 (0.9%)	16 (1.9%)	
CVA	6 (0.2%)	3 (0.2%)	7 (0.8%)	0.02
ST according to ARC definition††				
Definite or probable ST	24 (0.9%)	15 (1.1%)	15 (1.8%)	0.12
Acute	4 (0.2%)	3 (0.2%)	3 (0.2%)	
Subacute	16 (0.6%)	9 (0.6%)	8 (0.9%)	
Late	4 (0.2%)	3 (0.2%)	4 (0.5%)	
Definite ST	16 (0.6%)	9 (0.7%)	6 (0.7%)	0.95
Acute	4 (0.2%)	1 (0.1%)	1 (0.1%)	
Subacute	9 (0.3%)	6 (0.4%)	2 (0.2%)	
Late	3 (0.1%)	2 (0.1%)	3 (0.4%)	

*TVF: composite of cardiac death or MI attributable to target vessel, or TVR; **Kaplan-Meier estimates; †log-rank test; ††acute ST is defined as occurring within 24 h of stent implantation, subacute from 1 to 30 days, and late from 1 to 12 months.
TVF, target vessel failure; TLR, target lesion revascularization; TVR, target vessel revascularization; CVA, cerebrovascular accident; ST, stent thrombosis; ARC, Academic Research Consortium. Other abbreviations see in Table 1.

cularization of any segment of the index major coronary artery treated at the index procedure. Finally, bleeding was considered major when it lead to death or permanent disability, suspected or proven intracranial, produced a fall in haemoglobin >3 mmol/L, required transfusion of 2 or more units of whole blood (packed cells), or led to peripheral vascular surgery. All other bleeding was considered as minor. The following events were adjudicated by an independent clinical event committee whose members did not participate in the study: death, MI, TVR, TLR, and ST.

Statistical Analysis

Categorical variables were reported with counts and percentages and compared with the Chi-square test for trend; continuous variables were reported with the means and standard deviations (SD) (compared with 1-way ANOVA) or median and interquartile ranges (IQR). Cumulative event rates were estimated using the Kaplan-Meier method and compared with the log-rank test. Follow-up was censored at the last known date of follow-up, or at 12 months, whichever came first. Hazard ratios were calculated in Cox proportional-hazards models. For the outcome TLR, 3 sets of models were used: unadjusted using univariable analyses, adjusted multivariable with forced entry of established prognostic factors for in-stent-restenosis (lesion length, stent length, vessel diameter, post-treatment lumen diameter[13]), and adjusted multivariable using independent predictors identified by backwards selection of baseline and procedural variables. A P<0.1 by the likelihood ratio test was deemed significant. For the main outcome TVF, we performed unadjusted univariable analyses and adjusted multivariable using identified independent predictors for TVF.

As an exploratory analysis, the relation between the duration of DAPT and outcomes was investigated in an extended Cox model with DAPT entered as a time-dependent variable.

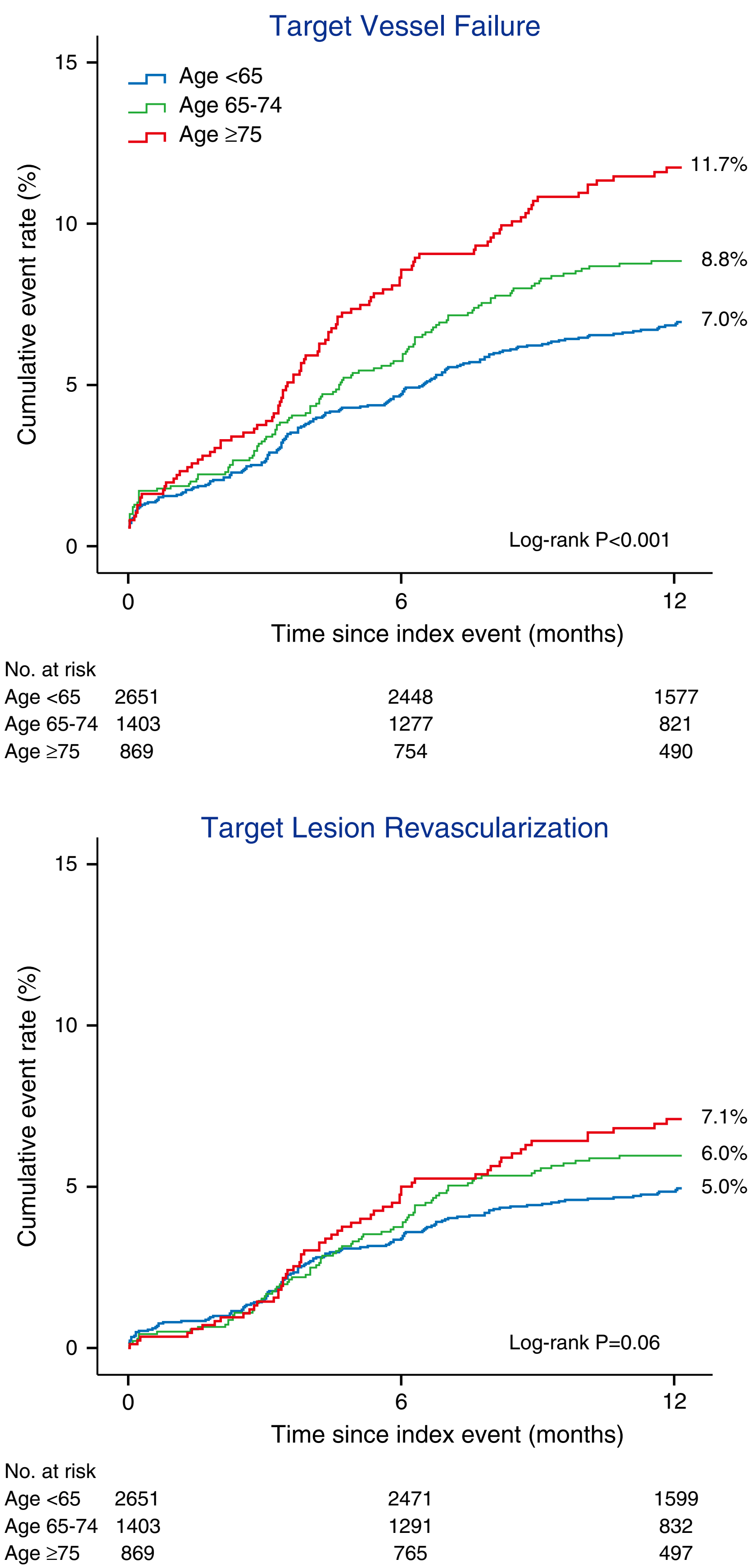

Figure. Kaplan-Meier curves for target vessel failure (**Upper**) and target lesion revascularization (**Lower**) according to age. Cumulative event rates are shown.

Table 4. Unadjusted and Adjusted HRs for TLR

	TLR HR (95%CI)	TLR P value
Unadjusted analysis		
Age		0.06
<65	Reference	–
65–74	1.21 (0.92–1.60)	0.18
≥75	1.44 (1.05–1.97)	0.02
Adjusted for established predictors		
Age		0.05
<65	Reference	–
65–74	1.24 (0.94–1.65)	0.13
≥75	1.47 (1.07–2.01)	0.02
Mean reference vessel diameter (mm)	0.58 (0.41–0.81)	0.01
Mean stent length (mm)	1.01 (0.98–1.04)	0.52
Mean lesion length (mm)	1.01 (0.99–1.03)	0.38
Mean diameter stenosis post-procedure (%)	1.00 (1.00–1.01)	0.28
Adjusted for identified predictors		
Age		0.38
<65	Reference	–
65–74	1.10 (0.83–1.46)	0.52
≥75	1.25 (0.91–1.73)	0.17
Insulin-dependent diabetes mellitus	1.58 (1.01–2.47)	0.047
Current smoker	0.71 (0.51–0.98)	0.04
History of congestive heart failure	0.28 (0.09–0.89)	0.03
Indication for PCI		
Elective	Reference	–
ACS	1.09 (0.85–1.40)	0.49
Other/unknown	0.47 (0.24–0.89)	0.02
Mean reference vessel diameter (mm)	0.60 (0.43–0.84)	<0.01
Minimal 1 B2 or C lesion treated	1.42 (1.10–1.83)	<0.01
Minimal 1 restenosis treated	2.04 (1.23–3.39)	<0.01
Minimal 1 bifurcation treated	1.44 (1.04–1.99)	0.03

HR, hazard Ratios; CI, confidence interval. Other abbreviations see in Tables 1,3.

In the case of discontinuation of DAPT, we assumed that there was no restart until the end of follow-up. In this time-dependent analysis, we included all elderly patients with known DAPT data.

Statistical analyses were performed at the Academic Medical Center of the University of Amsterdam.

Results

Patients

A total of 4,996 patients were entered in the e-HEALING registry, of which 52 patients were excluded because of missing procedure-related data (n=16), no Genous stent was placed or Genous placement was unknown (n=36). Five patients were excluded because of missing follow-up data. Of the remaining 4,939 patients, 2,651 were aged <65 years, 1,403 aged 65–74 years, 794 aged 75–84 years and 75 aged ≥85. Because of low patient numbers in the ≥85 age group, the 75–84 and ≥85 age groups were merged. The baseline characteristics of the patients across the various age categories are shown in **Table 1**. Generally, with increasing age, patients were more often female, had a lower body mass index, more often had hypertension and congestive heart failure and a more extensive history of revascularization. Hypercholesterolemia, current smoking and family history of MI occurred less frequently with increasing age.

The median time of follow-up of the total population was 365 days (IQR 358–365 days). The completeness of follow-up for clinical events was 98.9% at 30 days (±1 week), 97.1% at 6 months (±2 weeks), and 92.3% at 12 months (±4 weeks).

Angiographic and Procedural Characteristics

Detailed angiographic and procedural characteristics are shown in **Table 2**. Multivessel PCI was performed with increasing age, and the lesions were more complex as indicated by the ACC/AHA lesion classification B2/C lesions.

Outcomes

The main 12-month outcome of TVF occurred significantly more often in elderly patients compared with younger patients (7.0% in patients aged <65 years, 8.8% in patients aged 65–74 years and 11.7% in patients aged ≥75, P<0.001). The composite of death, MI or TLR occurred in 6.5% in patients aged <65 years, 8.5% in patients aged 65–74 years and 11.3% in patients aged ≥75, P<0.001). Both composite outcomes were mainly driven by a significantly higher mortality in the (very) elderly patients (P<0.001). We did not observe a significant difference in MI. There was a trend to higher TLR with increasing age (overall log-rank P=0.06). The bleeding rates at 12-month follow-up were more frequent with increasing age

(P<0.001). Regarding definite or probable ST, no significant difference was observed between the elderly and younger patients. The clinical outcomes, according to age category, are shown in detail in **Table 3**. Kaplan-Meier curves for TVF and TLR are shown in **Figure**. We analyzed TVF and definite or probable ST according to the indication for PCI. In patients aged <65, 65–74 and ≥75 years, TVF rates were respectively 6.9%, 10.3% and 10.3%, respectively, in elective PCI (P=0.02) and 7.6%, 8.3% and 13.2%, respectively, in PCI for acute coronary syndrome (ACS) (P<0.01). Definite or probable ST rates were 0.8%, 0.9% and 0.7%, respectively, in elective PCI (P=0.92) and 1.1%, 1.4% and 2.3%, respectively, in PCI for ACS (P=0.14). In order to facilitate the comparison with other studies, clinical outcomes according to the age ≥70 years and age ≥80 years are provided respectively in **Tables S1**,**S2**. Importantly, patients aged ≥70 years had a TLR rate of 6.5% and for patients aged ≥80 it was 8.0%.

Cox Proportional-Hazards Models

Univariable analysis showed that patients aged ≥75 had a higher TLR hazard to younger patients (HR 1.44, 95% confidence interval (CI) 1.05–1.97, P=0.02). The other age categories had comparable TLR hazards. These hazard ratios were not materially affected by adjustment for the established risk factors for TLR. In our dataset, the following variables were identified as significant predictors for TLR: insulin-dependent diabetes mellitus, current smoking, history of congestive heart failure, indication for PCI, mean reference vessel diameter, ≥1 lesion classified as ACC/AHA type B2 or C, ≥1 restenotic lesion treated, or ≥1 bifurcation treated (P<0.1 for all). After adjustment for these identified predictors, age lost its statistical significance. The unadjusted and adjusted models are shown in **Table 4**. After adjustment for identified risk factors (insulin-dependent diabetes mellitus, previous PCI, history of stroke, indication for PCI, mean reference vessel diameter, mean lesion length, minimal 1 restenosis or B2/C lesion or bifurcation, minimal 1 lesion with post-procedural TIMI 0–2 flow) for the main outcome TVF, the presence of age ≥75 (HR 1.47, 95%CI 1.14–1.90. P<0.01) was associated with a significantly higher TVF hazard when compared with age <65 years. Patients aged 65–74 years had a comparable TVF hazard (HR 1.17, 95%CI 0.93–1.48. P=0.19).

DAPT

Adherence to DAPT in the elderly (≥65 years) at 30-day, 6-month and 12-month follow-up was respectively 78.3%, 53.6% and 30.4%. In the time-dependent analysis, 2,031 patients were evaluated. No significant difference in TVF was observed when comparing continuation of DAPT with discontinuation of DAPT after adjustment for relevant predictors for TVF in these elderly (HR 1.37, 95%CI 0.89–2.09, P=0.15)

Discussion

We described the 12-month outcomes after Genous stent placement in elderly patients from the e-HEALING registry. The main findings of the study were as follows. We observed a significantly higher rate of TVF in the elderly, compared with younger patients, mainly driven by higher 12-month mortality in the elderly patients. Although there was a trend to higher TLR rates with increasing age, this relation weakened after adjustment for identified predictors for TLR. Thus TLR rates were dependent on variables other than age. There was no difference in ST between elderly and younger patients. Finally, bleeding rates were significantly higher in the elderly.

Previous Studies

In a pooled analysis of patients undergoing PCI with BMS placement, mortality and bleeding were significantly higher in patients aged ≥80 years.[2] Clinical restenosis was similar to that in younger patients (8% in age ≥80 years vs. 11% in younger patients at 1 year). Our current results corroborate these findings, with regards to the higher mortality and bleeding hazard. This is possibly explained by multiple comorbidities in the elderly patients. In contrast to the comparable TLR rate, we observed a trend to higher TLR with increasing age when we use the same 80-year cut-off. A possible explanation is the prevalence of more complex lesions in the elderly, as shown by the number of ACC/AHA classification B2/C lesions. After adjustments for other predictors of TLR, the relation between age and TLR was not longer statistically significant. On the other hand, there was no difference in insulin-dependent diabetics and small differences in visually assessed reference vessel diameter or lesion length in the very elderly subgroup. We previously identified insulin-dependence as a predictor for TLR.[14] Another explanation could be that in older patients the EPCs are increasingly impaired in terms of functional features such as proliferation, migration and survival.[15]

Regarding DES placement in the elderly, Vlaar et al report 12-month outcomes in octogenarians. Although major adverse cardiac events were significantly higher, no difference was observed in TLR (4.5% vs. 4.9% in younger patients).[16] A more recent publication regarding DES placement in the elderly concerns a pooled analysis of outcomes after paclitaxel-eluting stent placement.[17] In that analysis, registry patients aged 70 years or older showed low single-digit TLR rates at 2-year follow-up, which were lower than those observed in younger patients and explained by the authors as related to less aggressive atherosclerotic disease in the elderly. Altogether, our current study adds evidence to the current literature suggesting that the frequency of repeat revascularizations after coronary stenting is comparable with increasing age. However, the TLR rates in the very elderly need further investigation.

DAPT

Early discontinuation of DAPT has been identified as a major predictor for the occurrence of ST.[8] In e-HEALING, low rates of ST were observed despite the recommendation of 1 month of DAPT. In our elderly population, approximately 50% was still on DAPT at 6 months, and more than 25% was on DAPT at 12 months. This result may be influenced by the high percentage of patients treated for ACS included in the e-HEALING registry. We hypothesize that shorter DAPT use in the elderly patients would reduce the current significantly higher bleeding rate, without an increased ST risk, because of the safety of the Genous stent. In an exploratory analysis, duration of DAPT was not associated with TVF.

Clinical Implications

Literature regarding the use of DES in elderly patients is scanty because advanced age is an exclusion criterion in many clinical trials. We therefore emphasize the importance of direct comparisons of DES and Genous within this population, taking the optimal duration of DAPT into account. An important benefit of the Genous stent for the elderly is the low ST risk despite shorter DAPT. This safety benefit in terms of ST has to be weighed against the efficacy in terms of TLR. Importantly, in the TRIAS-HR randomized trial, non-inferiority of Genous compared with DES with regards to TVF at 1-year could not be established in lesions at high risk for restenosis.[18] High-risk lesions were defined as a lesion with a length ≥20 mm or reference vessel diameter ≤2.8 mm, a chronic coronary artery occlusion or any lesion in a diabetic patient. The higher TVF rate with Genous was mainly driven by TLR. Though no large differences were observed in these high-risk lesion characteristics in e-HEALING across the age groups, further research in the elderly should focus on the potential benefit in terms of a shorter duration of DAPT vs. the potential higher TLR risk with Genous. A recently published single-center study was concerned with the 1-year outcomes after Genous placement in patients aged 75 or older.[19] That study suggested that the Genous stent was safe and feasible in very elderly patients, with a low ST rate despite 1-month DAPT. Clinically justified TLR was frequently observed (22%). However, this high TLR rate can possibly be explained by the oculostenotic reflex, because 73% of the patients underwent angiographic follow-up at 6-month follow-up and 19 of the 22 clinically justified TLR occurred during this angiographic follow-up period.

Study Limitations

Some limitations of our present analysis deserve mention. The potential underreporting of adverse events is a potential important shortcoming of all large registries. The present study was organized with a comprehensive data-management plan that included frequent monitoring of all participating sites and full event verification designed to minimize the effects of event underreporting. In addition, 12 months of follow-up may be too short to accurately assess the risk of very late ST. Furthermore, because a proportion of the patients were on DAPT for more then 1 month, this could theoretically diminished the 12-month ST rate. Finally, angiographic variables were obtained by visual assessment.

Conclusions

The 1-year results of the Genous stent in a population of elderly patients show a significantly higher TVF rate compared with younger patients, mainly driven by a higher mortality. Although there was a trend to higher TLR rates with increasing age, there was no difference in ST between elderly and younger patients, which attests to the safety of this therapy for the elderly, in whom there could be concerns with administering long-term DAPT.

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All other authors declare that they have no conflict of interest.

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Supplemental Files

Supplemental File 1

Table S1. 12-Month Outcomes According to Age ≥70 Years or Younger

Table S2. 12-Month Outcomes According to Age ≥80 Years or Younger

Please find supplemental file(s);
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