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# Percutaneous coronary intervention of unprotected left main and bifurcation in octogenarians: Subanalysis from RAIN (veRy thin stents for patients with left mAIn or bifurcatioN in real life)

Federico Conrotto MD<sup>1</sup> | Fabrizio D'Ascenzo MD<sup>1</sup> | Francesco Piroli MD<sup>1</sup> |  
 Alfonso Franzé MD<sup>1</sup> | Leonardo de Luca MD<sup>2</sup> | Giorgio Quadri MD<sup>3</sup> |  
 Nicola Ryan MD<sup>4</sup> | Javier Escaned MD<sup>4</sup> | Mario Bo MD<sup>5</sup> |  
 Gaetano Maria De Ferrari MD<sup>1</sup>

<sup>1</sup>Division of Cardiology, Department of Internal Medicine, Città della Salute e della Scienza, Torino, Italy

<sup>2</sup>U.O.C. Cardiologia, Ospedale San Giovanni Evangelista, Rome, Italy

<sup>3</sup>Department of Cardiology, Infermi Hospital, Turin, Italy

<sup>4</sup>Department of Cardiology, Hospital Clinico San Carlos, Madrid, Spain

<sup>5</sup>Division of Geriatrics, Department of Internal Medicine, Città della Salute e della Scienza, Torino, Italy

**Correspondence**

Francesco Piroli, Division of Cardiology,  
 Department of Internal Medicine, Città della  
 Salute e della Scienza, Torino, Italy.  
 Email: francescopiroli@yahoo.it

**Abstract**

**Objective:** Outcomes of complex percutaneous coronary interventions (PCIs) in older patients are still debated.

The aim of the study was to evaluate clinical outcomes of Octogenarian patients treated with ultrathinstents on left main or on coronary bifurcations, compared with younger patients.

**Methods:** All consecutive patients presenting a critical lesion of an unprotected left main (ULM) or a bifurcation and treated with very thin stents were included in the RAIN (veRy thin stents for patients with left mAIn or bifurcatioN in real life) registry and divided into octogenarians group (OG, 551 patients) and nonoctogenarians (NOGs, 2,453 patients). Major adverse cardiovascular event (MACE), a composite end point of all-cause death, nonfatal myocardial infarction (MI), target lesion revascularization (TLR), and stent thrombosis (ST), was the primary endpoint, while MACE components, cardiovascular (CV) death, and target vessel revascularization (TVR) were the secondary ones.

**Results:** Indication for PCI was acute coronary syndrome in 64.7% of the OG versus 53.1% of the NOG. Severe calcifications and a diffuse disease were significantly more in OG. After a follow-up of 15.2 ± 10.3 months, MACEs were higher in the OG than in the NOG patients (OG 19.1% vs. NOG 11.2%,  $p < .001$ ), along with MI (OG 6%

**Abbreviations:** ACC, American College of Cardiology; ACS, acute coronary syndrome; AHA, American Heart Association; CABG, coronary artery bypass graft; CI, confidence interval; CV, cardiovascular; DAPT, double antiplatelet therapy; EF, ejection fraction; ESC, European Society of Cardiology; FKB, final kissing balloon; FFR, fractional flow reserve; IVUS, intravascular ultrasound; MACE, major adverse cardiac events; MI, myocardial infarction; NOG, nonoctogenarian group; OCT, optical coherence tomography; OMT, optimal medical therapy; OG, octogenarian group; OR, odds ratio; PCI, percutaneous coronary intervention; ST, stent thrombosis; STE, ST elevation; TLR, target lesion revascularization; TVR, target vessel revascularization; ULM, unprotected left main.

vs. NOG 3.4%,  $p = .002$ ) and all-cause death (OG 14% vs. NOG 4.3%,  $p < .001$ ). In contrast, no significant difference was detected in CV-death (OG 5.1% vs. NOG 4%,  $p = .871$ ), TVR/TLR, or ST. At multivariate analysis, age was not an independent predictor of MACE (OR 1.02 CI 95% 0.76–1.38), while it was for all-cause death, along with diabetes, GFR < 60 ml/min, and ULM disease.

**Discussion:** Midterm outcomes of complex PCI in OG are similar to those of younger patients. However, due to the higher non-CV death rate, accurate patient selection is mandatory.

#### KEYWORDS

bifurcations, elderly, left main, octogenarians, PCI

## 1 | INTRODUCTION

In Western world, the percentage of population over 80 years is increasingly growing: according to Eurostat,<sup>1</sup> nowadays there are 27.3 million people aged 80 years and over in the European Union, 7 million more than that 10 years ago.

Older age is a well-known predictor for coronary artery disease (CAD) and cardiovascular events.<sup>2,3</sup> Data from the GRACE registry<sup>4</sup> showed that patients older than 75 years represent one fourth of those hospitalized with acute coronary syndrome (ACS), whereas the Oxford Vascular Study demonstrated that 47% of the acute coronary events occurred in 6% of the population aged 75 years and over.<sup>5</sup> Elderly patients with ACS have worse prognosis compared with younger patients.<sup>6,7</sup> Age, comorbidities, frailty, cognitive impairment, functional disability, and reduced use of medical and procedural guidelines-recommended treatments have been demonstrated to be associated with increased cardiovascular (CV) and all-cause death in older patients.<sup>6–10</sup>

Percutaneous coronary intervention (PCI) becomes more challenging in elderly patients because of peripheral artery disease, diffuse coronary disease, tortuosity of vessels, calcified lesions, low ejection fraction (EF), risk of bleeding, and comorbidities.<sup>11</sup> Previous studies suggested that these factors are associated with a twofold to fourfold increased risk of negative clinical outcomes, including mortality, myocardial infarction (MI), need for revascularization, stroke, renal failure, and major bleeding.<sup>12–14</sup> For these reasons, in current clinical practice, physicians opt more frequently for a conservative management in the elderly,<sup>15,16</sup> despite several evidence of potential clinical benefit from PCI<sup>17–20</sup> and despite the guidelines recommendations.<sup>21</sup>

In randomized trials, patients with lesions involving bifurcations or unprotected left main (ULM), as well as octogenarian patients, are under-represented. Last generation ultrathin stents have represented a changing scenario for complex PCI, due to in vitro evidence of reduced shear stress, potentially leading to decreased risk of stent thrombosis and restenosis. On this background, we analyzed the RAIN (veRy thin stents for patients with left mAIn or bifurcatioN in real life, NCT03544294),<sup>22</sup> a retrospective multicenter study, to evaluate clinical outcomes of octogenarian patients treated with ultrathin stents on LM or on coronary bifurcations, compared with younger patients.

## 2 | METHODS

We performed a reanalysis of the RAIN,<sup>22</sup> a retrospective multicenter study (see Appendix web only for sites of enrollment) including patients from June 2015 to January 2017.

All consecutive patients presenting with a critical lesion of ULM or involving a bifurcation (see Appendix web only for definition) in our centers were included, if treated with one of the following stents:

- Platinum–chromium stent coated with a permanent polymer loading everolimus with strut thickness of 81  $\mu\text{m}$  for diameters from 2.25 to 3.5 mm and of 86  $\mu\text{m}$  for a diameter of 4.0 mm (Promus Element™, Boston Scientific).

- Cobalt-chromium stent coated with a biodegradable polymer abluminal coating loading sirolimus with strut thickness of 80  $\mu\text{m}$ ; (Ultimaster™, Terumo Corporation);

- Platinum–chromium stent coated with a biodegradable polymer loading everolimus with strut thickness of 74  $\mu\text{m}$  for diameters in the range 2.25–2.75 mm, 79  $\mu\text{m}$  for diameters in the range 3.00–3.50 mm, and 81  $\mu\text{m}$  for diameters equal to 4.0 mm; (Synergy™, Boston Scientific);

- Cobalt–chromium stent coated with a permanent polymer loading everolimus with a strut thickness of 80  $\mu\text{m}$  (Xience Alpine™, Abbott);

- Platinum–chromium stent coated with a biodegradable polymer loading zotarolimus with a strut thickness of 74  $\mu\text{m}$  for diameters  $\leq 2.5$  mm, 79  $\mu\text{m}$  for diameters in the range 3.0–3.50 mm, and 81  $\mu\text{m}$  for diameter equal to 4.0 mm (Resolute Onyx™, Medtronic);

- Cobalt–chromium stent coated with a biodegradable polymer loading biolimus with a strut thickness of 84  $\mu\text{m}$  (Biomatrix Alpha™, Biosensors).

Patients were divided into two groups: octogenarians (OG) if they were  $\geq 80$  years old, and nonoctogenarian (NOG) if they were <80 years old at the time of the procedure.

Data about cardiovascular risk factors, clinical presentation, angiographic features, use of intravascular ultrasound (IVUS), optical coherence tomography (OCT), and fractional flow reserve (FFR) were collected along with characteristics of implanted stents. Data were derived from electronic charts at each center on prespecified forms and recorded online (<http://www.cardiogroup.org/RAIN/index.php?cat=home>). Postdilatation, final kissing balloon (FKB), use of imaging,

**TABLE 1** Shows baseline characteristics in the higher part (Panel A), procedure results in the middle (Panel B), and outcomes at follow-up in the lower part (Panel C)

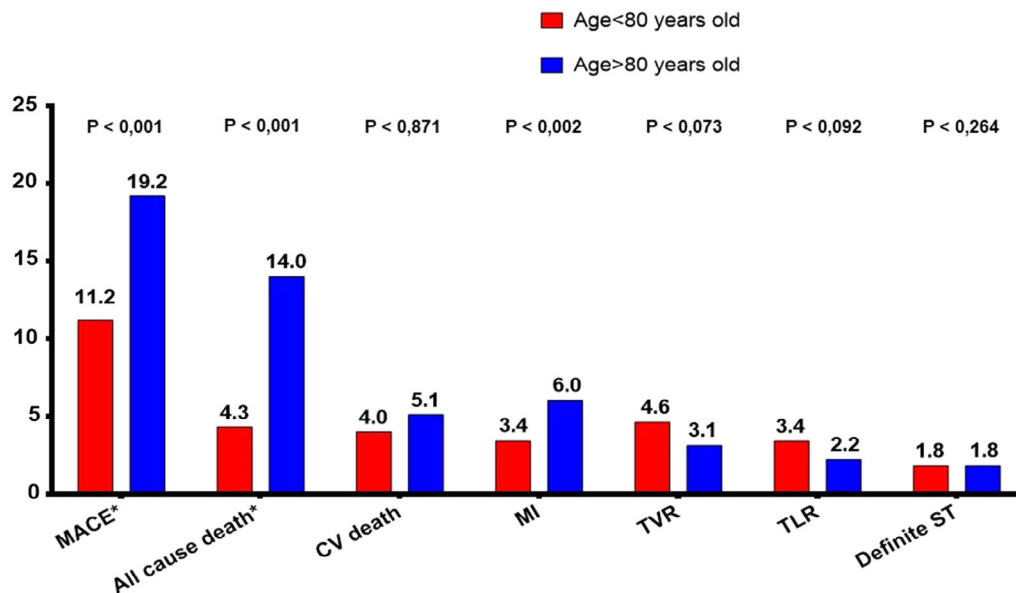
	NOG	OG	p-values
Panel A: Baseline characteristics			
Total of patients	82 (2,453/3,004)	18 (551/3,004)	—
Age in years (mean ± SD)	64.8 ± 11	83.55 ± 3.07	—
Male	78.4 (1,923/2,453)	66.1 (364/551)	<.001
Hypertension	72.7 (1,736/2,387)	83.6 (449/537)	<.001
Diabetes mellitus non-ID	24.3 (580/2,386)	27.7 (148/536)	.122
Diabetes mellitus ID	7.6 (156/2,064)	7.5 (34/452)	.979
Hyperlipidemia	60.6 (1,445/2,386)	57.5 (308/536)	.188
Smoker	30.1 (710/2,361)	25.9 (136/525)	.046
Previous smoker	23.8 (563/2,361)	7.2 (38/525)	<.001
GFR < 60 ml/min	16.4 (367/2,237)	38.10 (190/499)	<.001
Previous PCI	32s.8 (791/2,415)	29 (158/544)	.094
Previous CABG	4.9 (117/2,412)	5.5 (30/544)	.521
Previous MI	28.4 (666/2,349)	33.4 (177/530)	.021
ACS	53.1 (1,292/2,434)	64.7 (353/546)	<.001
STEMI	17.3 (421/2,434)	15.4 (84/546)	.313
NSTEMI	21.8 (530/2,434)	34.2 (187/546)	<.001
UA	14 (341/2,434)	15 (82/546)	.542
Stable angina	26.3 (641/2,434)	22.2 (121/546)	.045
Positive stress test	13.3 (323/2,434)	8.8 (48/546)	.004
Planned	7.2 (176/2,434)	4 (23/546)	.01
Other	0 (1/2,434)	0.2 (1/546)	.333
ASA + clopidogrel	63.9 (1,442/2,258)	75.3 (384/510)	<.001
ASA + ticagrelor	27.4 (618/2,258)	21.8 (111/510)	<.009
ASA + prasugrel	8.6 (194/2,258)	2.9 (15/510)	<.001
Other drugs	0.18 (4/2,258)	0 (0/510)	1
DAPT < 12 months	13.31 (250/1,878)	14.53 (60/413)	.525
DAPT ≥ 12 months	86.69 (1,628/1,878)	85.47 (353/413)	
Length in months (average ± SD)	11.52 ± 9.71	10.85 ± 3.07	.164
Panel B: Procedure results			
Radial access	70.2 (1,675/2,385)	62.2 (337/542)	.001
Femoral access	29.7 (709/2,385)	37.8 (205/542)	
Other	0 (1/2,385)	0 (0/542)	
Left main lesion	25.3 (605/2,393)	34.1 (185/542)	.001
Left anterior descending lesion	47.8 (1,145/2,393)	43.2 (234/542)	
Circumflex/marginal lesion	18.3 (439/2,393)	14.8 (80/542)	
Right coronary lesion	6.7 (161/2,393)	7 (38/542)	
Intermediate coronary lesion	1.8 (42/2,393)	0.9 (5/542)	
Other	0 (1/2,393)	0 (0/542)	
Bifurcations	87.38 (2,091/2,372)	84.69 (459/539)	.06
Type C lesion	38.9 (855/2,196)	37.7 (188/499)	.602
Severe calcification	11.4 (235/2,067)	21.4 (104/487)	<.001
Diffuse disease	36 (804/2,236)	44.8 (230/513)	<.001
Predilatation	88.3 (2,014/2,282)	90.8 (472/520)	.107
Rotablator	2 (42/2,083)	4.5 (21/462)	.002
Postdilatation	74.2 (1,424/1,920)	73.7 (309/419)	.859

(Continues)

**TABLE 1** (Continued)

	NOG	OG	p-values
IVUS	32 (774/2,419)	34.7 (189/545)	.353
OCT	1 (23/2,419)	1.3 (7/545)	
Panel C: Outcomes			
MACE	11.2 (252/2,259)	19.1 (100/524)	<.001
Death	4.3 (98/2,262)	14 (73/523)	<.001
CV death	4 (90/2,262)	5.1 (27/523)	.871
Reinfarction	3.4 (83/2,453)	6 (33/551)	.002
Target vessel revascularization	4.6 (113/2,453)	3.1 (17/551)	.073
Target lesion revascularization	3.4 (83/2,453)	2.2 (12/551)	.092
Stent thrombosis	1.8 (43/2,453)	1.8 (10/551)	.264

Abbreviations: ACS, acute coronary syndrome; ASA, acetylsalicylic acid; CABG, coronary artery bypass graft; CV, cardiovascular; DAPT, double antiplatelet therapy; GFR, glomerular filtration rate; ID, insulin dependent; IVUS, intravascular ultrasound; MACE, major adverse cardiovascular events; MI, myocardial infarction; NOG, nonoctogenarian group; NSTEMI, non-ST-elevation myocardial infarction; OCT, optical coherence tomography; OG, octogenarian group; PCI, percutaneous coronary intervention; SD, standard deviation; STEMI, ST-elevation myocardial infarction.



**FIGURE 1** Incidence of outcomes at follow-up according to age group. Data are expressed in percentage. CV, cardiovascular; MI, myocardial infarction; MACE, major adverse cardiovascular events; ST, stent thrombosis; TLR, target lesion revascularization; TVR, target vessel revascularization [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

and choice of stenting techniques (provisional vs. 2-stents) were left to physicians' choice.

Follow-up was performed through dedicated clinical assessment, telephonic follow-up, or formal query to primary care physicians.

Endpoints of the study were major adverse cardiac events (MACEs), defined as composite end point of all-cause death, MI, target lesion revascularization (TLR), and stent thrombosis (ST), along with MACE single components, CV death, and target vessel revascularization (TVR).

Categorical variables are reported as count and percentages, whereas continuous variables as mean and SD. Gaussian or non-Gaussian distribution was evaluated by Kolmogorov-Smirnoff test. The t-test has been used to assess differences between parametric continuous variables, Mann-Whitney *U* test for nonparametric

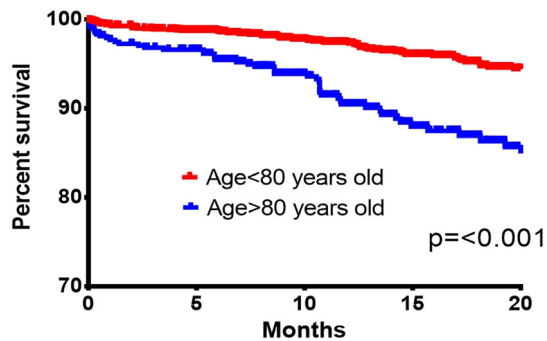
variables, the chi-square test for categorical variables, and Fisher exact test for  $2 \times 2$  tables. Cox multivariate analysis was performed to assess the independent predictors of MACE and of all-cause death. Proportional hazards assumption was not violated in statistical analysis. A two-sided *p*-value <.05 was considered statistically significant. All analyses were performed with SPSS 21.0 (IBM, Armonk, NY).

### 3 | RESULTS

Between June 2015 and January 2017, a total of 3,004 patients were enrolled in the RAIN retrospective multicenter study. These patients were divided into two groups:

- Nonoctogenarian group (NOG): 2,453 patients with age <80 years at the time of PCI (mean age of  $65.3 \pm 9.45$  years)
- Octogenarian group (OG): 551 patients with age  $\geq 80$  years, (mean age of  $83.55 \pm 3.07$  years)

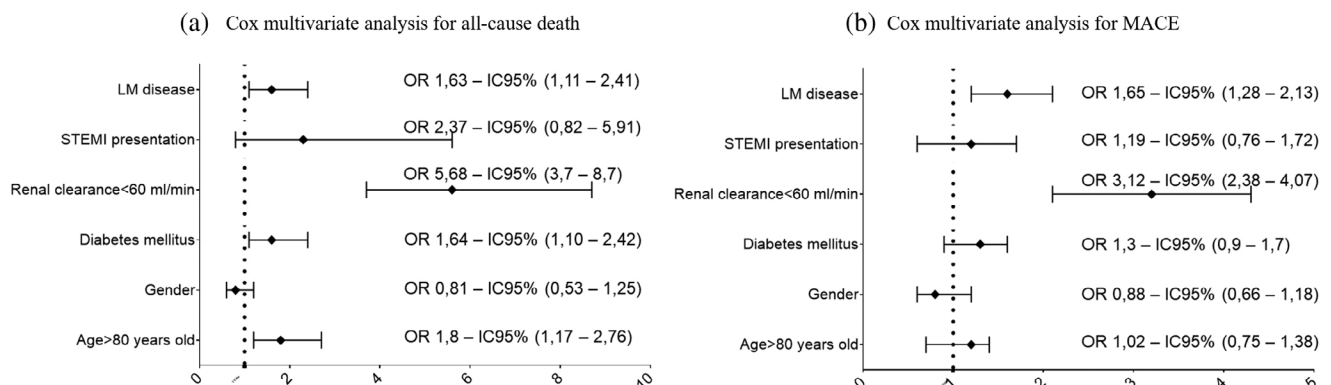
Baseline characteristics of our population are given in Table 1. Male gender was more represented in the younger group (OG 66.1% vs. NOG 78.6%,  $p < .001$ ), along with a higher proportion of current ( $p = .046$ ) and previous smokers ( $p < .001$ ) while hypertension (OG 83.6% vs. NOG 72.7%  $p < .001$ ) and a glomerular filtration rate lower than 60 ml/min (OG 38.1% vs. NOG 16.4%,  $p < .001$ ) were detected more frequently in elderly patients, who also reported a higher prevalence of previous MI (OG 33.4% vs. NOG 28.4%,  $p = .021$ ). ACS as an indication for PCI was more frequently observed in older than in younger patients (OG 64.7% vs. NOG 53.1%,  $p < .001$ ), driven by a higher percentage of NSTEMI (OG 34.2% vs. NOG 21.8%,  $p < .001$ ). There was a higher usage of ASA + clopidogrel in the elderly (OG 75.3% vs. NOG 63.9%,  $p < .001$ ), while a stronger P2Y12 inhibition with ticagrelor or prasugrel was chosen more frequently in the younger group. The length of DAPT was similar between the two groups (OG  $10.85 \pm 3.07$  months vs. NOG  $11.52 \pm 9.71$  months,  $p = .164$ ).



**FIGURE 2** Shows Kaplan-Meier plot for survival according to age group [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

Procedural characteristics are given in Table 1 (Panel B). The radial artery was the preferred access site in both groups, with a significantly higher percentage in the younger one (OG 62.2% vs. NOG 70.2%,  $p = .001$ ). LM angioplasty was performed in 34.1% of elderly patients and in 25.3% of younger patients. On the other hand, in the latter group, there was a higher prevalence of left anterior descending and circumflex coronary artery revascularization. Bifurcations were performed with similar rates (OG 84.7% vs. NOG 87.4%,  $p = .06$ ). Elderly patients underwent more complex procedures, with a significantly higher proportion of lesions with severe calcification (OG 21.4% vs. NOG 11.4%,  $p < .001$ ), and of rotablator usage (OG 4.5% vs. NOG 2%,  $p < .002$ ). Moreover, a diffuse disease was present in 44.8% of the elderly group versus 36% of the younger group ( $p < .001$ ). No significant differences were identified in the proportion of Type C lesions, as well as in the usage of intracoronary imaging techniques.

As shown in Figure 1 and in Panel C of Table 1, after a mean follow-up of  $15.2 \pm 10.3$  months, the rate of MACE resulted significantly higher in patients aged 80 years or older (OG 19.1% vs. NOG 11.2%  $p < .001$ ), along with the rate of MI (OG 6% vs. NOG 3.4%  $p = .002$ ) and of all-cause deaths (OG 14% vs. NOG 4.3%  $p < .001$ ) (see Kaplan-Meier plot, Figure 2). In contrast, no significant differences were detected between the two groups in terms of CV-death (OG 5.1% vs. NOG 4%,  $p = .871$ ), TVR, TLR (respectively  $p = .073$  and  $.092$ ), and ST ( $p = .264$ ). Figure 3 shows results of Cox multivariate analysis for all-cause death and MACE, including age  $> 80$  years, LM disease, percentage of STEMI presentation, GFR  $< 60$  ml/min, diabetes mellitus, and gender. Age  $\geq 80$  years (OR 1.8, CI 95% 1.17–2.76), GFR  $< 60$  ml/min (OR 5.68, CI 95% 3.7–8.7), diabetes mellitus (OR 1.64, CI 95% 1.1–2.42), and the presence of left main disease (OR 1.63, CI 95% 1.10–2.41) were correlated with all-cause death (Figure 3a). In contrast, age  $\geq 80$  years did not result to be an independent predictor of MACE (OR 1.02 CI 95% 0.76–1.38) (Figure 3b). The same trend was noted also after age stratification (see Table 2); age  $\geq 80$  years compared with age  $< 60$  years increased the risk of all-cause death (OR 2.49, CI 95% 1.39–4.4) but not of MACE (OR 1.22, CI 95% 0.85–1.75). Other classes of age did not increase the risk of death or MACE.



**FIGURE 3** Cox multivariate analysis for (a) all-cause death and (b) major adverse cardiovascular events. LM, left main; MACE, major adverse cardiovascular events; OR, odds ratio; STEMI, ST-elevation myocardial infarction

**TABLE 2** Multivariate analysis according to age stratification

MACE				
	<i>p</i> -value	OR	LCI	UCI
60 < age < 70 <sup>a</sup>	.187	0.786	0.549	1.124
70 ≤ age < 80 <sup>a</sup>	.677	0.931	0.664	1.305
≥80 <sup>a</sup>	.284	1.220	0.848	1.754
Diabetes mellitus	.005	1.406	1.105	1.789
Renal clearance < 60 ml/min	.000	2.613	2.038	3.349
LM disease	.008	1.387	1.088	1.768
STEMI	.001	1.593	1.197	2.119
Female gender	.722	1.051	0.800	1.380
All-cause death				
60 < age < 70 <sup>a</sup>	.398	1.148	0.627	2.100
70 ≤ age < 80 <sup>a</sup>	.894	1.041	0.573	1.893
≥80 <sup>a</sup>	.002	2.498	1.395	4.473
Diabetes mellitus	.001	1.762	1.258	2.467
Renal clearance < 60 ml/min	.000	4.809	3.348	6.907
LM disease	.023	1.506	1.058	2.145
STEMI	.000	3.071	2.126	4.436
Female gender	.623	1.101	0.751	1.612

Abbreviations: LCI, lower confidence interval; LM, left main; MACE, major adverse cardiovascular events; OR, odds ratio; STEMI, ST elevation myocardial infarction; UCI, upper confidence interval.

<sup>a</sup>≤60 years old as referral.

## 4 | DISCUSSION

The findings of this retrospective study demonstrated that, compared with younger subjects, patients aged ≥80 years (a) had a more complex coronary disease (diffuse, calcified and involving the left main), along with a higher prevalence of ACS, previous MI, hypertension and chronic kidney disease and (b) suffered from a significantly higher rate of MACEs, mainly driven by a more than threefold increased risk all-cause death and a slight but significant increased risk of MI, while cardiovascular death rates were consistent with younger patients. Also age ≥ 80, GFR < 60 ml/min, diabetes mellitus, and the presence of left main disease were found to be independent predictors of all-cause-death in the Cox multivariate analysis, while age was not a predictor of MACE.

The feasibility of PCI in octogenarians, despite the higher complexity of lesions (two times more plaques with severe calcifications, and 1.24 times more diffuse disease in our study), was already reported by Miura et al.<sup>23</sup>: although patients aged over 80 years, compared with younger patients, presented with more calcified lesions and a higher syntax score, the angiographic success rate was similar in the two groups.

In our study elderly patients underwent ULM-PCI procedures more frequently than younger patients. Indeed, only a small proportion of these very elderly, complex, and comorbid patients might be a candidate for surgical revascularization, whereas CABG may be a reasonable alternative treatment for a greater proportion of younger patients. In an observational study, Nicolini et al.<sup>24</sup> compared PCI

versus CABG in patients aged below and over 80 years, showing no difference in 30-day mortality, and lower mortality for CABG in the follow-up. These long-term results could be probably affected by a pretest bias because only particular healthy octogenarians can withstand general anesthesia and CABG surgery. In our previous study<sup>25</sup> about PCI versus CABG on ULM in octogenarians, we found no difference in the primary composite endpoint (death, cardiovascular accident, MI) between the two strategies; however, the rate of TVR was higher in the PCI group.

In the present study, the clinical indication leading to PCI is one of the major points of difference between the two groups, with ACS being significantly more frequent in elderly than in younger patients (OG 64.7% vs. NOG 53.1%, *p* < .001). Elderly people, due to their reduced physical activity, often do not develop symptoms until the plaque burden becomes severe. Even positive stress tests are fewer because their execution on common treadmill often is not feasible for orthopedic diseases. These differences led to less invasive procedures for stable angina and more for ACS, and obviously, this factor can negatively influence the outcomes in the OG. On the other hand, elderly people who develop exertion angina probably are a particular healthy subgroup of this population, which has much to gain in terms of quality of life. This point is important because the aim of coronary intervention in the setting of stable angina in the elderly patient is symptom relief, with no prognostic benefit, as demonstrated by the TIME trial.<sup>19</sup> In contrast, in NSTEMI-ACS setting, performing a routine invasive strategy in older patients gives benefits in terms of mortality,<sup>26-28</sup> which has been

quantified by Batch et al.<sup>29</sup> in an absolute risk reduction of 10.8 percentage points (10.8% vs. 21.6%;  $p = .016$ ).

In our study, we found no significant difference in the percentage of STEMI between the two groups. Even in this setting, data from the EUROTRANSFER Registry<sup>30</sup> and from the TRIANA<sup>31</sup> and the PAMI<sup>32</sup> trials show that elderly patients have a higher mortality than younger patients, but routine invasive strategy improves death, reinfarction, and stroke. The Belgian STEMI registry,<sup>15</sup> enrolling 1,092 octogenarians over 7,984 patients, reveal that the main negative prognostic factor in elderly STEMI patients is cardiac failure, since the mortality benefit of PCI over OMT was maintained in hemodynamically stable octogenarians. Another factor influencing negatively outcomes after STEMI in older people is the atypical presentation of symptoms, since this can cause diagnosis and treatment delays.<sup>33</sup> ESC<sup>21</sup> and ACC/AHA<sup>34</sup> guidelines recommend the same management of younger patients in the setting of STE-ACS.

One of the major findings of our study is that octogenarians, despite a higher prevalence of ACS and NSTEMI, along with a more complex coronary disease (diffuse, calcified, and involving the left main), have similar rates of cardiovascular deaths, while all-cause death was significantly more frequent. Despite the higher rate of MACE shown in the OG, age was not an independent predictor of MACE at the Cox multivariate analysis. Even TVR and TLR showed similar results in both groups. These findings suggest that PCI with limus stent is actually a safe and effective procedure also in very elderly patients and in complex procedures like ULM and bifurcations, with cardiovascular outcomes similar to younger patients. However, postprocedural age- and comorbidity-associated complications occur more frequently in elderly patients, thereby leading to increased all-cause mortality in older patients. Our findings are in keeping with results from previous studies. In a sample of 1,657 patients with STEMI, hospitalized during the period 2008–2014, who underwent primary PCI, those aged  $\geq 75$  years had long-term mortality more than four-fold higher compared with younger patients.<sup>35</sup> Data from the CRUSADE registry showed that one-year mortality in patients who survived a NSTEMI increased markedly with age, from 13.3% for patients aged 65–79 years to 45.5% for those aged  $\geq 90$  years.<sup>36</sup> Comorbidities, frailty, cognitive impairment, functional disability have been demonstrated to be associated with increased CV and all-cause death in older patients with ACS<sup>6–10,37,38</sup> or in stable CAD,<sup>39,40</sup> and there is some evidence that PCI might be an effective procedure also in complex frail elderly patients.<sup>41</sup> Patient's age and the presence of comorbidities have been historically used as surrogates of frailty, even if there is poor correlation between these elements.<sup>42</sup> Unfortunately, in this retrospective study, patient-centered variables with well-known prognostic implications in elderly patients (including comorbidity, frailty, cognitive impairment, and functional disability) were not collected. Although findings from the present study underscore the unmet need of patients centered selection criteria to identify older patients who might derive the greatest benefit versus those with uncertain benefit from invasive procedures, there are currently no definitive evidences in this regard. However, in

the STORM study, we demonstrated that the use of the Gold Standards Framework (GSF) may independently predict non CV death in patients with ACS thereby identifying those approaching the end of life and with very uncertain benefit from invasive procedures.<sup>43</sup>

From our Cox multivariate analysis, regardless of age, two important comorbidities emerge as predictors of all-cause death: diabetes mellitus and kidney failure. Previous studies<sup>44–46</sup> have quantified a minimum of twofold increase in the mortality rate in patients with these comorbidities. Intensive glycemic, lipid, and blood pressure control, in addition to prehydration with normal saline at the time of procedure, remain the only methods of proven efficacy to improve outcomes.<sup>46,47</sup>

Finally, ESC/AHA guidelines<sup>48–50</sup> recommend an individual management of elderly patients, possibly with a heart team including geriatric specialists, in order to weigh risk–benefit ratio, evaluating frailty, symptomatic ischemia, bleeding risk, life expectancy, comorbidities, cognitive function, quality of life and, not least, patient wishes.

The present article presents some limitations. The absence of data on contrast medium did not allow any analysis regarding its impact on in-hospital adverse events like acute kidney injury. Moreover, the RAIN data set comprises only patients undergoing PCI, consequently not allowing any comparison with patients treated with medical therapy only.

## 5 | CONCLUSIONS

In octogenarians, performing complex PCI, like those of ULM and bifurcations, is feasible and associated with the same rate of cardiovascular mortality, TVR, TLR, and ST of younger patients, even if comorbidities negatively influence survival. Cornerstones for proper indication to revascularization are a correct selection of the patient, along with a multidimensional evaluation, in collaboration with geriatric specialists.

### ORCID

Fabrizio D'Ascenzo  <https://orcid.org/0000-0002-6646-9317>

Francesco Piroli  <https://orcid.org/0000-0001-6817-2923>

Giorgio Quadri  <https://orcid.org/0000-0003-4164-2758>

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**How to cite this article:** Conrotto F, D'Ascenzo F, Piroli F, et al. Percutaneous coronary intervention of unprotected left main and bifurcation in octogenarians: Subanalysis from RAIN (veRy thin stents for patients with left mAln or bifurcatioN in real life). *Catheter Cardiovasc Interv*. 2020;1-9. <https://doi.org/10.1002/ccd.29048>