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Patterns of in-hospital mortality and bleeding complications following PCI for very elderly patients: insights from the Dartmouth Dynamic Registry

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Abstract

Background Very elderly patients (age ≥ 85 years) are a rapidly increasing segment of the population. As a group, they experience high rates of in-hospital mortality and bleeding complications following percutaneous coronary intervention (PCI). However, the relationship between bleeding and mortality in the very elderly is unknown. **Methods** Retrospective review was performed on 17,378 consecutive PCI procedures from 2000 to 2015 at Dartmouth-Hitchcock Medical Center. Incidence of bleeding during the index PCI admission (bleeding requiring transfusion, access site hematoma > 5 cm, pseudoaneurysm, and retroperitoneal bleed) and in-hospital mortality were reported for four age groups (< 65 years, 65–74 years, 75–84 years, and ≥ 85 years). The mortality of patients who suffered bleeding complications and those who did not was calculated and multivariate analysis was performed for in-hospital mortality. Lastly, known predictors of bleeding were compared between patients age < 85 years and age ≥ 85 years. **Results** Of 17,378 patients studied, 1019 (5.9%) experienced bleeding and 369 (2.1%) died in-hospital following PCI. Incidence of bleeding and in-hospital mortality increased monotonically with increasing age (mortality: 0.94%, 2.27%, 4.24% and 4.58%; bleeding: 3.96%, 6.62%, 10.68% and 13.99% for ages < 65, 65–74, 75–84 and ≥ 85 years, respectively). On multivariate analysis, bleeding was associated with increased mortality for all age groups except patients age ≥ 85 years [odds ratio (95% CI): age < 65 years, 3.65 (1.99–6.74); age 65–74 years, 2.83 (1.62–4.94); age 75–84 years, 3.86 (2.56–5.82), age ≥ 85 years: 1.39 (0.49–3.95)]. **Conclusions** Bleeding and mortality following PCI increase with increasing age. For the very elderly, despite high rates of bleeding, bleeding is no longer predictive of in-hospital mortality following PCI.

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Keywords: Complications; In-hospital mortality; Percutaneous coronary intervention; The elderly

1 Introduction

The very elderly (age ≥ 85 years) is a rapidly growing segment of our population. The prevalence of coronary artery disease (CAD) increases with age, reaching 30.6% in male patients over the age of 80 and 21.7% in female patients over 80.[1] Accordingly, there is an increasing number of percutaneous coronary interventions (PCI) in this population.[2,3] Previous studies had shown that very elderly patients have a higher risk of both bleeding and in-hospital mortality, but it is unclear to what extent bleeding contributes to in-hospital mortality in this age group.[4,5]

Bleeding following PCI is associated with an increased incidence of adverse outcomes such as non-fatal myocardial infarction (MI), stroke, and prolonged hospital stay.[6,7] In addition, previous studies using the National Cardiovascular Data Registry (NCDR) CathPCI database have shown that bleeding complications are associated with in-hospital mortality.[8] This increased risk of in-hospital mortality in the context of bleeding has not been validated in the very elderly. In addition, approaches designed to reduce bleeding complications such as bivalirudin anticoagulation in place of heparin, arterial closure device use, and radial artery access have an uncertain impact on mortality in the very elderly.[9–11]

Very elderly patients likely have a unique risk profile when undergoing PCI that remains incompletely defined. The objective of this study was to examine the relationship between bleeding and mortality in the very elderly undergoing PCI.

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2 Methods

2.1 Study population

After obtaining approval from our institution's Committee for the Protection of Human Subjects, we queried the Dartmouth Dynamic Registry for all consecutive PCI cases between 2000 and 2015. Baseline demographics of age, sex, smoking status, hypertension, hyperlipidemia, diabetes, kidney disease, and previous PCI were collected. Patients who had missing demographic or outcomes data were excluded from the study.

2.2 Outcomes and covariates

Primary outcomes were in-hospital mortality and composite bleeding, which was defined as any of the following: bleeding requiring transfusion, access site hematoma size greater than 5 cm, pseudoaneurysm, arterial injury requiring vascular surgery repair, or retroperitoneal bleed confirmed by CT scanning. The primary outcomes were reported for four age groups: < 65 years, 65–74 years, 75–84 years, and ≥ 85 years. Within each of the four age groups, in-hospital mortality was calculated for patients who experienced bleeding and those who did not. Predictors of bleeding and in-hospital mortality were compared for patients age < 85 years and ≥ 85 years. Previously identified predictors of bleeding used in this study include: sex, presentation with acute coronary syndrome (ACS), cardiogenic shock, cardiac arrest, estimated glomerular filtration rate (eGFR) < 30 mL/min, previous PCI, and baseline diagnosis of congestive heart failure (CHF).[8] Previously identified predictors of in-hospital mortality used in this study include: diabetes mellitus, eGFR < 30 mL/min, previous PCI, baseline diagnosis of CHF, chronic obstructive pulmonary disease (COPD), left main intervention, presentation with cardiogenic shock, and ST elevation myocardial infarction (STEMI).[12]

2.3 Statistical analysis

Categorical variables were summarized as frequencies and percentages and continuous variables were summarized as means and standard deviations. Chi-square test was used to determine statistical difference between categorical variables. The independent impact of bleeding on in-hospital mortality was assessed by multivariate logistic regression for the four age groups. Covariates in the multivariate analysis included presentation with cardiogenic shock or STEMI, baseline diagnosis of CHF, and eGFR < 30 mL/min.[12] Statistical significance was defined as a two- sided P value < 0.05. All statistical analysis was performed using STATA version 13.1.

3 Results

Data was collected for 17,599 consecutive PCI procedures between 2000 and 2015 at Dartmouth-Hitchcock Medical Center. Due to missing demographic data, 221 procedures were excluded from the analysis yielding the total analytic cohort of 17,378 procedures. The baseline demographic and procedural characteristics of the study population are shown in Table 1. Of the total study population, 1019 (5.9%) experienced bleeding and 369 (2.1%) died during the index hospitalization. Very elderly patients had a low incidence of smoking (27%) and diabetes (21%), and infrequently underwent PCI as an elective procedure (14%).

Incidences of bleeding were 3.9%, 6.6%, 10.7%, and 13.9%, and incidences of in-hospital mortality were 0.9%, 2.3%, 4.2%, and 4.5% respectively for patients age < 65, 65–74, 75–84, and ≥ 85 years (Figure 1). Among patients who experienced bleeding, patients age ≥ 85 years had a lower incidence of in-hospital mortality than patients age 65–74 years and age 75–84 years (Figure 2). For patients age ≥ 85 years, in-hospital mortality was not significantly different between those who experienced bleeding and those who did not [7.27% *vs*. 4.14%; risk difference: 3.13% (95% CI: −1.95%–8.21%)] (Table 2). Similarly, on multivariate analysis, patients age ≥ 85 years who experienced bleeding did not have significantly higher odds ratio for mortality than patients who did not experience bleeding [odds ratio: 1.2 (95% CI: 0.5–3.0)] (Table 3).

For patients age < 85 years, those who bled were more frequently female, had a greater incidence of diabetes mellitus, COPD, eGFR < 30 mL/min, CHF, and previous PCI. They also presented more frequently with cardiogenic shock, cardiac arrest, STEMI, left main stenosis, and less frequently for elective procedures. For patients age ≥ 85 years, those who bled had a higher incidence of diabetes mellitus, eGFR < 30 mL/min, CHF, cardiogenic shock, but were similarly likely to be female, received previous PCI, present with cardiac arrest, STEMI, or have an elective procedure (Tables 4 & 5).

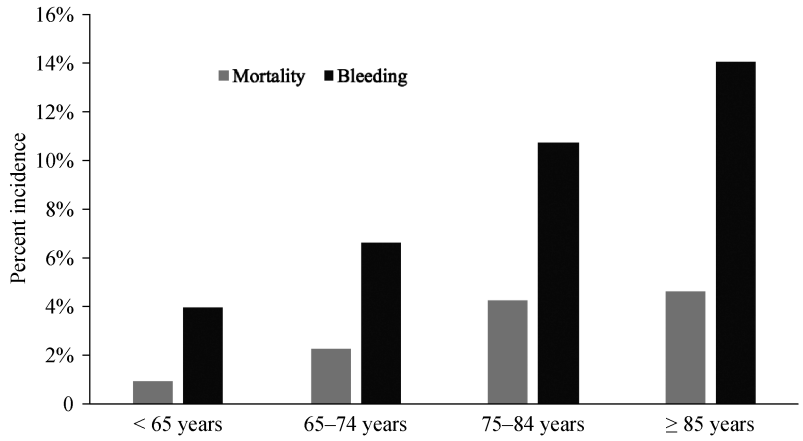
4 Discussion

In our study of 17,378 PCI procedures, PCI in the very elderly (≥ 85 years) represented a small fraction of all PCI (4.5%). In-hospital mortality and bleeding increased monotonically with increasing age. Moreover, among patients who experienced bleeding, very elderly patients had lower in-hospital mortality (7.3%) than patients age 65–74 years (12.5%) and patients age 75–84 years (17.0%). Lastly, for the very elderly, we found there was no independent relationship between bleeding and mortality.

Table 1. Demographics and procedural characteristics.

	Age < 65 yrs (*n* = 8461)	Age 65–74 yrs (*n* = 4712)	Age 75–84 yrs (*n* = 3419)	Age > 85 yrs (*n* = 786)	*P*-value
Female	2494 (31%)	1370 (29%)	1016 (30%)	208 (26%)	0.026†
Smoking	5109 (65%)	2207 (47%)	1242 (36%)	209 (27%)	< 0.001*,†
Hypertension	5219 (66%)	3431 (71%)	2623 (77%)	625 (80%)	0.069*†
Hyperlipidemia	5631 (71%)	3316 (70%)	2284 (67%)	462 (59%)	< 0.001*,†
Diabetes	2317 (29%)	1604 (34%)	989 (29%)	168 (21%)	< 0.001*,†
eGFR < 30 mL/min	452 (6%)	277 (6%)	248 (7%)	57 (7%)	NS†
EF < 35%	699 (9%)	312 (7%)	288 (4%)	82 (10%)	< 0.001*
Previous PCI	2373 (30%)	1432 (30%)	983 (29%)	219 (28%)	NS
COPD	583 (6.8%)	618 (13.1%)	471 (13.8%)	94 (12.0%)	NS†
Presentation and procedural characteristics					
Cardiac arrest	212 (3%)	73 (2%)	56 (2%)	15 (2%)	NS
Cardiogenic shock	97 (1%)	81 (2%)	87 (3%)	15 (2%)	NS
STEMI	1628 (21%)	595 (13%)	383 (11%)	126 (16%)	< 0.001*,†
Elective procedure	2315 (29%)	1451 (31%)	810 (24%)	112 (14%)	< 0.001*,†
Left main intervention	127 (1.5%)	164 (3.5%)	179 (5.2%)	54 (6.9%)	NS*†
Anticoagulation					
GPIIb/IIIa inhibitor	2640 (31%)	1228 (26%)	850 (25%)	161 (21%)	0.018*,†
Bivalirudin	5348 (63%)	2730 (58%)	1996 (58%)	465 (59%)	NS†

Data are presented as *n* (%) unless other indicated. *P*-value for comparison between age > 85 years and ages 75–84 years; *Indicates $P < 0.05$ when comparing age > 85 years with ages 65–74 years; †indicates $P < 0.05$ when comparing age > 85 years with age < 65 years. COPD: chronic obstructive pulmonary disease; EF: ejection fractions; eGFR: estimated glomerular filtrate rate; GPIIb/IIIa: glycoprotein IIb/IIIa; PCI: percutaneous coronary interventions; STEMI: ST elevation myocardial infarction.



	< 65 years	65–74 years	75–84 years	≥ 85 years
Mortality	26 (0.9%)	107 (2.3%)	145 (4.2%)	36 (4.6%)
Bleeding	342 (3.9%)	312 (6.6%)	365 (10.7%)	110 (13.9%)
Bleeding requiring transfusion	178 (2.1%)	184 (3.9%)	256 (7.5%)	78 (9.9%)
Hematoma	156 (1.8%)	135 (2.9%)	118 (3.5%)	35 (4.5%)
Pseudoaneurysm	17 (0.2%)	13 (0.3%)	29 (0.9%)	8 (1.0%)
Retroperitoneal Bleed	38 (0.4%)	22 (0.5%)	23 (0.7%)	5 (0.6%)

Figure 1. Incidence of bleeding and in-hospital mortality for patients undergoing PCI stratified by age (< 65, 65–74, 75–84 and ≥ 85 years). PCI: percutaneous coronary interventions.

The increasing trend of mortality and bleeding with age suggest that risk factors accumulated in one's lifetime directly impact PCI outcomes. More broadly, this can be viewed as a loss of physiologic reserve with increasing age. Interestingly, certain risk factors that traditionally have first order relationships with lifestyle (e.g., smoking, diabetes) are less common in the very elderly, but other risk factors such as renal dysfunction and heart failure are more common. It is likely that individuals surviving into their 8th and 9th decades possess a combination of favorable genetics as well as healthy lifestyle choices. Hence, it is not surprising that the very elderly have fewer of these risk factors. De-

spite this, as patients age, their risk of in-hospital mortality and bleeding increases.

For patients age < 85 years, the odds ratio of in-hospital mortality for patients who experience bleeding ranges from 2.8 to 3.8, which is consistent with previous studies on the

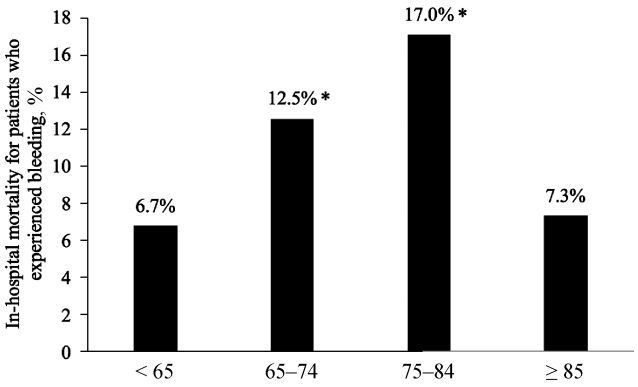


Figure 2. In-hospital mortality of patients who experienced bleeding complication following PCI stratified by age (< 65, 65–74, 75–84, ≥ 85 years). *Indicates significant difference (P < 0.05) when compared to age ≥ 85 years. PCI: percutaneous coronary interventions.

Table 2. In-hospital mortality for patients who experienced bleeding complications and those who did not.

Age, yrs	No bleeding	Bleeding	*P*-value	Risk difference	95% CI
< 65	58 (0.7%)	23 (6.7%)	< 0.001	6.0%	3.4%–8.7%
65–74	68 (1.5%)	39 (12.5%)	< 0.001	11.0%	7.3%–14.6%
75–84	83 (2.7%)	62 (17%)	< 0.001	14.3%	10.4%–18.2%
≥ 85	28 (4.1%)	8 (7.3%)	0.13	3.1%	–2.0%–8.2%

Table 3. Unadjusted and adjusted odds ratio for in-hospital mortality for patients who experienced bleeding.

Age, yrs	Odds Ratio	95% CI lower	95% CI upper	*P*-value
Unadjusted				
< 65	10.2	6.2	16.8	< 0.001
65–74	9.1	6.0	13.7	< 0.001
75–84	7.3	5.2	10.4	< 0.001
≥ 85	1.8	0.8	4.1	0.15
Adjusted				
< 65	3.7	2.0	6.7	< 0.001
65–74	2.8	1.6	4.9	< 0.001
75–84	3.9	2.6	5.8	< 0.001
≥ 85	1.2	0.5	3.0	0.76

Table 4. Predictors of bleeding for patients age < 85 and ≥ 85 years.

	No bleeding (*n* = 15,753)	Bleeding (*n* = 1019)	*P*-value	Risk difference	95% CI
Age < 85 yrs					
Sex (% female)	4539 (28.8%)	341 (33.5%)	0.002	4.7%	1.8%–7.5%
eGFR < 30 mL/min	820 (5.2%)	157 (15.4%)	< 0.001	10.2%	8.7%–11.6%
CHF	1567 (9.9%)	271 (26.6%)	< 0.001	16.7%	14.7%–18.6%
Previous PCI	4532 (28.8%)	256 (25.1%)	0.013	–3.6%	–6.5%– –0.8%
Presentation characteristics					
Cardiac arrest	281 (1.8%)	60 (5.9%)	< 0.001	4.1%	3.2%–4.9%
Cardiogenic shock	172 (1.0%)	105 (10.3%)	< 0.001	9.3%	8.4%–10.0%
STEMI	2410 (15.3%)	196 (19.2%)	< 0.001	3.9%	1.6%–6.2%
Elective Procedure	4472 (28.4%)	104 (10.2%)	< 0.001	–18.2%	–21.0%– –15.4%
	No bleeding (*n* = 676)	**Bleeding(*n* = 110)**	***P*-value**	**Risk difference**	**95% CI**
Age ≥ 85 yrs					
Sex (% female)	179 (26.5%)	29 (26.3%)	0.96	–0.2%	–9.0%–8.8%
eGFR < 30 mL/min	44 (6.5%)	13 (11.8%)	< 0.001	5.3%	0.8%–10.5%
CHF	157 (23.2%)	40 (36.4%)	< 0.001	13.2%	0.2%–10.5%
Previous PCI	186 (27.5%)	33 (30.0%)	0.59	2.5%	–6.6%–11.5%
Presentation characteristics					
Cardiac arrest	11 (1.7%)	4 (3.6%)	0.16	2.0%	–0.8%–4.8%
Cardiogenic shock	9 (1.3%)	6 (5.5%)	< 0.001	4.1%	1.4%–6.9%
STEMI	108 (15.9%)	18 (16.3%)	0.91	0.3%	–7.0%–7.8%
Elective procedure	102 (15.1%)	10 (9.1%)	0.09	–6.0%	–0.1%–10.5%

Data are presented as *n* (%) unless other indicated. CHF: congestive heart failure; eGFR: glomerular filtration rate; PCI: percutaneous coronary intervention; STEMI: ST elevation myocardial infarction.

Table 5. Predictors of in-hospital mortality for patients age < 85 years and ≥ 85 years.

	No bleeding (*n* = 15753)	Bleeding (*n* = 1019)	*P*-value	Risk difference	95% CI
Age < 85 yrs					
Diabetes mellitus	4558 (28.9%)	352 (34.5%)	< 0.001	5.6%	2.7%–8.5%
eGFR < 30 mL/min	820 (5.21%)	157 (15.4%)	< 0.001	10.2%	8.7%–11.6%
CHF	1567 (9.94%)	271 (26.6%)	< 0.001	16.7%	14.7%–18.6%
Previous PCI	4532 (28.8%)	256 (25.1%)	0.01	-3.6%	–6.5%–0.8%
COPD	1529 (9.7%)	143 (14.0%)	< 0.001	4.3%	2.4%–6.2%
Presentation characteristics					
Left main intervention	382 (2.42%)	88 (8.6%)	< 0.001	6.2%	5.2%–7.3%
Cardiogenic shock	172 (1.02%)	105 (10.3%)	< 0.001	9.3%	8.4%–10.0%
STEMI	2410 (15.3%)	196 (19.2%)	< 0.001	3.9%	1.6%–6.2%
	No bleeding (*n* = 676)	**Bleeding (*n* = 110)**	***P*-value**	**Risk difference**	**95% CI**
Age ≥ 85 yrs					
Diabetes mellitus	136 (20.1%)	32 (29.1%)	0.03	9.0%	0.7%–17.2%
eGFR < 30 mL/min	44(6.5%)	13 (11.8%)	< 0.001	5.3%	0.8%–10.5%
CHF	157 (23.2%)	40 (36.4%)	< 0.001	13.2%	0.2%–10.5%
Previous PCI	186 (27.5%)	33 (30.0%)	0.59	2.5%	–6.6%–11.5%
COPD	77 (11.4%)	17 (15.5%)	0.22	4.1%	–2.5%–10.6%
Presentation characteristics					
Left main intervention	43 (6.4%)	11 (10.0%)	0.15	3.6%	–1.5%–8.7%
Cardiogenic shock	9 (1.33%)	6 (5.45%)	< 0.001	4.1%	1.4%–6.9%
STEMI	108 (15.9%)	18 (16.3%)	0.91	0.3%	–7.0%–7.8%

Data are presented as *n* (%) unless other indicated. CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; eGFR: estimated glomerular filtration rate; PCI: percutaneous coronary intervention; STEMI: ST elevation myocardial infarction.

impact of bleeding on in-hospital and long term mortality for the general population.[8,13,14] In a sub-analysis of the ACUITY trial, Manoukian, *et al*.[6] demonstrated that among patients with ACS, those who experienced major bleeding had a higher rate of 30-day mortality—a finding confined to the ACS population. Similarly, in a large retrospective analysis of the NCDR data, Chhatriwalla, *et al*.[8] showed that bleeding was associated with higher mortality across the spectrum of bleeding risk. These studies however, did not specifically investigate the relationship between bleeding and mortality for the very elderly. In our study, for patients aged ≥ 85 years, bleeding was not associated with increased in-hospital mortality. While this result is contrary to what has been published about the impact of bleeding on in-hospital mortality with advancing age, our study uniquely investigates the relationship for the very elderly (age ≥ 85 years).

One explanation for the lack of association between bleeding and mortality in the very elderly is that the increased incidence of bleeding is not uniquely related to the morbidity of the procedure, but also by the fact that very elderly patients are more likely to bleed from multiple causes. In other words, bleeding is more prevalent in the very elderly and no longer discriminates between who is going to live and who is not. Patients aged < 85 years who experienced bleeding had a higher incidence of many (8) predictors for bleeding when compared to their counterparts who did not experience bleeding. On the other hand, patients aged ≥ 85 years who experienced bleeding had a higher incidence of fewer (3) predictors of bleeding. This suggests that for the very elderly, patients who experience bleeding and those who do not, have a more homogenous distribution of risk factors for bleeding. This homogeneity serves to dilute the association between bleeding and in-hospital mortality seen in younger patients. The fact that in-hospital mortality among patients who experienced bleeding is lower for patients age ≥ 85 years compared to younger patients supports this hypothesis. If very elderly and low bleeding risk patients are experiencing bleeding without an impact on in-hospital mortality, it is conceivable that this phenomenon will reduce the incidence of in-hospital mortality compared to younger patients. A similar pattern was also seen when comparing the predictors of in-hospital mortality between patients who experienced bleeding and those who did not. Predictors of in-hospital mortality were more common in patients who bled for patients age < 85 years but less so in those age ≥ 85 years. In the context of age's association with in-hospital mortality, another possi-

ble explanation for the lack of association between bleeding and mortality for the very elderly is that very elderly patients have increasing number of threats to their mortality that are independent from bleeding complications and that this weakens the relationship between bleeding and mortality.

As the population ages and the volume of PCI performed on very elderly patients increases, it is important to clearly define risk for this population. This study demonstrates that for the very elderly, the expected increased incidence of bleeding shouldn't absolutely preclude PCI. However, the link between age and in-hospital mortality is strong, and this higher mortality needs to be considered in the decision to proceed with PCI. If bleeding does not significantly impact mortality for the very elderly, it is likely other factors do. It is conceivable that frailty in the very elderly patient manifests in a greater set of potential threats to life, each of which may dilute the impact of bleeding on mortality. Hence, very elderly patients likely have a unique risk profile that requires further investigation.

There are limitations to this retrospective analysis. A major driver of the composite bleeding outcome is bleeding requiring transfusion. Since transfusion itself introduces morbidity, it is possible that there were confounding impacts of transfusion not accounted for in the study model. Furthermore, variables not included in the multivariate analysis may affect the association between bleeding and in-hospital mortality. Selection bias for healthier patients in the very elderly patients could have altered the findings as well. Importantly, the sample size of patients age ≥ 85 years is small and we lack the statistical power to definitively state the absence of an independent relationship between bleeding and in-hospital mortality in the very elderly. Our findings will need to be validated in a larger prospective study.

In conclusion, bleeding and in-hospital mortality following PCI increase with increasing age. Despite the association between bleeding and mortality in most age groups, bleeding in the very elderly is not associated with increased in-hospital mortality following PCI.

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