International Journal of Cardiology 151 (2011) 164–169

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Predictors of hospital mortality in the elderly undergoing percutaneous coronary intervention for acute coronary syndromes and stable angina☆

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ARTICLE INFO

Article history:
Received 20 January 2010
Received in revised form 5 May 2010
Accepted 13 May 2010
Available online 3 June 2010

Keywords:
Percutaneous coronary intervention
Age
Mortality
Predictors

ABSTRACT

Background: The percentage of elderly treated with percutaneous coronary intervention (PCI) has been increasing year by year. Little is known about predictors of hospital mortality in elderly undergoing PCI for acute coronary syndromes (ACS) and stable angina.

Methods: Between 2005 and 2008 a total of 47,407 consecutive patients undergoing PCI were prospectively enrolled into the PCI-Registry of the EHS Programme. For the present analysis patients were divided into four categories: ACS patients ≥75 (n=4,943) and <75 years (n=19,446), and patients with stable angina ≥75 (n=3,393) and <75 years (n=19,625). A multiple logistic regression analysis was conducted to detect independent predictors of mortality in patients ≥75 years undergoing PCI. In addition, differences in clinical characteristics, procedural details and in-hospital outcomes between the subgroups were evaluated.

Results: Patients ≥75 years had more co-morbidities, and more severe coronary pathology. The use of guideline-recommended adjunctive therapy and procedural success was high in all groups. The incidence of in-hospital death was highest in ACS patients ≥75 years (5.2%) and <75 years (1.7%), followed by patients with stable angina ≥75 (0.5%) and <75 years (0.2%). Haemodynamic instability and acute ST-elevation myocardial infarction were the strongest determinants of hospital mortality among patients ≥75 years with ACS, whereas interventional complications were the most meaningful predictors of death in older patients undergoing elective PCI.

Conclusions: Patients ≥75 years undergoing PCI face a relatively low risk of hospital death. However, complication rates were significantly higher compared to younger patients, strongly influenced by clinical, angiographic and interventional variables.

1. Introduction

New methods for prevention and treatment of cardiovascular diseases have improved outcomes and increased life expectancy. An increasing number of elderly patients therefore require subsequent medical and interventional therapy. This is a challenge for modern cardiology since past documentation of clinical practice indicates that the management of elderly patients often differs from that of younger patients [1–6]. Furthermore, elderly cardiac patients, particularly those with severe co-morbidities, have been underrepresented in randomized clinical trials relative to their disease prevalence [7].

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doi:10.1016/j.ijcard.2010.05.006

Elderly undergoing PCI are at higher risk for complications compared to younger patients, emphasizing the growing importance of investigating periprocedural modalities and prognostic factors [8–10]. In the past determinants of mortality have been investigated in elderly patients undergoing PCI [8,10]. However, angiographic and procedural variables were not incorporated in these analyses.

Within the large Euro Heart Survey PCI Registry, which enrolled patients from 2005 until 2008, the current practice in patients of two age groups (≥75 and <75 years) with and without ACS was compared. For the first time preprocedural, angiographic and interventional factors predictive of mortality in patients ≥75 years undergoing PCI were determined. In contrast to previous investigations patients with ACS and stable angina were analyzed separately.

2. Methods

2.1. The PCI-Registry of the Euro Heart Survey Programme

The PCI-Registry is a prospective, multi-centre, observational study on current practice of unselected patients undergoing elective or emergency PCI. Consecutive patients with ACS or stable coronary artery disease (CAD) were recruited within the period from May 2005 to April 2008. The participating hospitals were located throughout Europe (176 centres in 33 ESC countries) and included university hospitals, community hospitals, specialist cardiology centres and private hospitals all providing PCI.

During the specified period all patients treated with PCI were prospectively registered, and followed during their clinical course, to document patient characteristics, adjunctive medical treatment, procedural details and in-hospital outcomes. Every participating centre was committed to include every consecutive patient undergoing PCI during selected time periods. All patients gave written informed consent for processing their anonymous data. Electronic case report forms were used for data entry and transferred via the web to a central database located in the European Heart House, where they were edited for missing data, inconsistencies and outliers. Additional editing of the data as well as the statistical analyses for this publication was performed at the Institut fuer Herzinfarktforschung Ludwigshafen an der Universitaet Heidelberg, Germany. The study was approved by the ethics committees responsible for the participating centres as required by local rules.

2.2. Definitions

Post ST elevation myocardial infarction (STEMI) was defined in the presence of the following criteria: onset of symptoms >24 h before PCI and with or without fibrinolysis. Bleeding complications were classified as major when the patient had an intracranial bleed or an overt clinical bleeding with a drop in haemoglobin of greater than 5 g/dl. Chronic renal failure was diagnosed by any of the following: serum creatinine >2 mg/dl or 200 μmol/l in the past, on dialysis or history of renal transplantation.

2.3. Statistical methods

Categorical data are presented as absolute numbers and percentages, metrical data as medians with 25th and 75th percentiles. The frequencies of categorical variables in two populations were compared by Pearson χ^2 test and by calculating odds-ratios (OR) and 95% confidence intervals (CI). Continuous and ordinal variables were compared by Mann–Whitney–Wilcoxon test. Descriptive statistics were calculated from the available cases.

The effect of age on periprocedural mortality was explored by stratification into intervals. The group of patients aged 40–50 years had the lowest mortality risk and was defined as the reference group. Odds ratios were estimated with adjustment for gender, haemodynamic instability, ACS, prior myocardial infarction, diabetes and chronic renal failure. Furthermore, we evaluated the impact of different baseline, angiographic and procedural variables on hospital mortality among patients ≥75 years with ACS as well as elective patients by using multiple logistic regression models and calculating the odds ratios with 95% confidence intervals. The following three groups of variables were incorporated in multivariate regression analysis, on the basis of preselection by clinical considerations and secondly the bi-variate association with hospital mortality ($p<0.2$ for all included variables): 1) the patient characteristics known before the procedure (haemodynamic instability [=cardiogenic shock and/or resuscitation], acute STEMI,

Table 1
Baseline characteristics

	ACS			Elective		
	Age ≥ 75 yrs. $n=4{,}943$	Age <75 yrs. $n=19{,}446$	*P*-value	Age ≥ 75 yrs. $n=3{,}393$	Age <75 yrs. $n=19{,}625$	*P*-value
Demographics						
Age (mean)	80.1 ± 3.8	59.6 ± 9.7	<0.0001	78.8 ± 3.1***	60.9 ± 8.9	<0.0001
Women	44.4%	22.2%	<0.0001	37.9%***	22.6%	<0.0001
Weight [kg/m²]	72 (65–80)	80 (70–90)	<0.0001	75(67–82)***	80 (72–90)	<0.0001
History relevant to cad						
Prior MI	30.4%	25.5%	<0.0001	37.7%***	41.8%	<0.0001
Prior PCI	18.6%	16.5%	<0.001	32.0%***	31.4%	ns
Prior CABG	8.0%	4.5%	<0.0001	10.6%***	6.9%	<0.0001
Congestive heart failure	10.0%	5.9%	<0.0001	17.0%***	15.6%	<0.05
Valvular heart disease	4.2%	1.5%	<0.0001	4.1%	2.0%	<0.0001
History of stroke	8.3%	3.6%	<0.0001	6.3%**	3.2%	<0.0001
PAD	9.4%	5.3%	<0.0001	8.7%	5.5%	<0.0001
Chronic renal failure	7.2%	2.7%	<0.0001	6.4%	2.7%	<0.0001
Risk factors						
Hypertension	74.6%	61.3%	<0.0001	80.0%***	73.2%	<0.0001
Diabetes mellitus	27.8%	23.5%	<0.0001	27.4%	25.4%	<0.0001
Hypercholesterolemia	51.5%	57.7%	<0.0001	67.1%***	72.9%	<0.0001
Current/former smoker	28.9%	61.3%	<0.0001	29.8%	53.1%	<0.0001
PCI indication and initial assessment						
STEMI/primary PCI	28.8%	29.9%	ns	–	–	–
STEMI/rescue PCI	1.2%	2.6%	<0.0001	–	–	–
STEMI/facilitated PCI	0.7%	1.4%	<0.0001	–	–	–
Post STEMI	8.2%	12.1%	<0.0001	–	–	–
NSTEMI	30.4%	24.2%	<0.0001	–	–	–
Unstable Angina	30.7%	29.8%	ns	–	–	–
Cardiogenic shock	4.3%	3.0%	<0.0001	–	–	–
Resuscitation	3.1%	3.3%	ns	–	–	–
Left ventricular function						
EF >50%	54.9%	63.9%	<0.0001	74.4%***	76.8%	<0.05
EF <30%	7.5%	4.6%	<0.0001	3.0%***	2.5%	ns

* $P<0.05$ ≥ 75 yrs. ACS vs. ≥ 75 yrs. elective.
** $P<0.001$ ≥ 75 yrs. ACS vs. ≥ 75 yrs. elective.
*** $P<0.0001$ ≥ 75 yrs. ACS vs. ≥ 75 yrs. elective.

Table 2
Angiographic and interventional characteristics.

	ACS			Elective		
	Age ≥ 75 yrs. $n=4,943$	Age <75 yrs. $n=19,446$	P-value	Age ≥ 75 yrs. $n=3,393$	Age <75 yrs. $n=19,625$	P-value
Stenosed vessels (≥50%)						
Left main stem	7.6%	3.5%	<0.0001	6.7%	4.4%	<0.0001
≥2 vessels	68.5%	53.3%	<0.0001	57.3%***	47.8%	<0.0001
Treated vessels						
Left main stem	4.2%	1.9%	<0.0001	3.8%	3.0%	<0.05
Left anterior descending	49.5%	48.0%	ns	49.0%	49.4%	ns
≥2 vessels	15.7%	14.2%	<0.05	18.7%**	17.5%	ns
Bypass	3.0%	1.5%	<0.0001	2.5%	1.6%	<0.001
Lesion characteristics						
Type C	33.1%	30.1%	<0.0001	26.9%***	26.1%	ns
In-stent restenosis	5,8%	5.4%	ns	7.5%*	8.1%	ns
Bifurcation	17.1%	15.4%	<0.05	16.7%	15.5%	ns
Therapeutic devices						
Bare-metal stent	62.0%	57.7%	<0.0001	53.4%***	51.8%	ns
Drug-eluting stent	34.9%	40.6%	<0.0001	46.3%***	47.9%	ns
Procedural success						
TIMI 3 flow after PCI	91.0%	92.4%	<0.01	94.0%***	94.4%	ns
<50% stenosis after PCI	94.0%	95.8%	<0.0001	94.6%	94.7%	ns
Acute segment closure	0.7%	0.6%	ns	0.7%	0.4%	<0.05
Coronary perforation	0.5%	0.3%	ns	0.5%	0.2%	<0.05
Antithrombotic treatment before or during PCI						
Aspirin	79.3%	80.9%	<0.05	77.3%	80.3%	<0.0001
Clopidogrel	74.4%	77.6%	<0.0001	76.8%*	80.0%	<0.001
Ticlopidine	2.7%	3.3%	ns	5.2%***	5.1%	ns
GP IIb/IIIa antagonist	26.9%	33.6%	<0.0001	15.9%***	16.8%	ns
Unfractionated heparin	85.4%	85.1%	ns	80.4%***	78.2%	<0.05
LMWH	30.1%	32.0%	<0.05	19.3%***	21.5%	<0.05
Antiplatelet therapy at discharge						
Aspirin	91.1%	92.4%	<0.05	91.9%	92.5%	ns
Clopidogrel	90.5%	90.7%	ns	91.2%	89.7%	<0.05
Ticlopidine	4.8%	5.4%	ns	5.2%	5.4%	ns

*$P<0.05$ ≥ 75 yrs. ACS vs. ≥ 75 yrs. elective.
**$P<0.001$ ≥ 75 yrs. ACS vs. ≥ 75 yrs. elective.
***$P<0.0001$ ≥ 75 yrs. ACS vs. ≥ 75 yrs. elective.

non ST elevation myocardial infarction [NSTEMI], chronic renal failure, history of stroke, congestive heart failure, peripheral vascular disease, diabetes, female gender, and age [per 5-year increase]); 2) the angiographic characteristics (3-vessel disease, left main disease, left anterior descending [LAD] stenosis, Type C lesion); and 3) the interventional characteristics (TIMI flow <3 after PCI, acute segment closure, and coronary perforation). Among patients ≥75 years with elective PCI the number of deaths was small, we derived clinical summary indices for preprocedural (preprocedural index) (age ≥ 80 years, weight <65 kg, valvular heart disease, LVEF <30%, diabetes mellitus), angiographic (angiographic index) (left main disease, type C lesion, bypass graft) and interventional (interventional index) (TIMI<3after PCI, acute segment closure, coronary perforation) information by counting the present characteristics within the three groups. The discrimination of the models was assessed with the C-statistics (0.87, respectively).

P-values ≤0.05 were considered significant. All p-values are results of two-tailed tests. The analysis was performed with the SAS© system release 9.1 on a personal computer (SAS Institute, Inc., Cary, North Carolina).

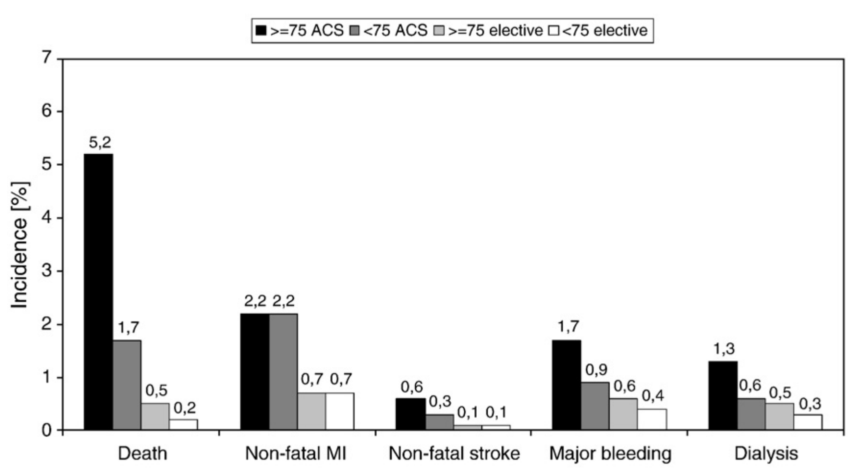

Fig. 1. Hospital complications in patients aged ≥75 and <75 years.

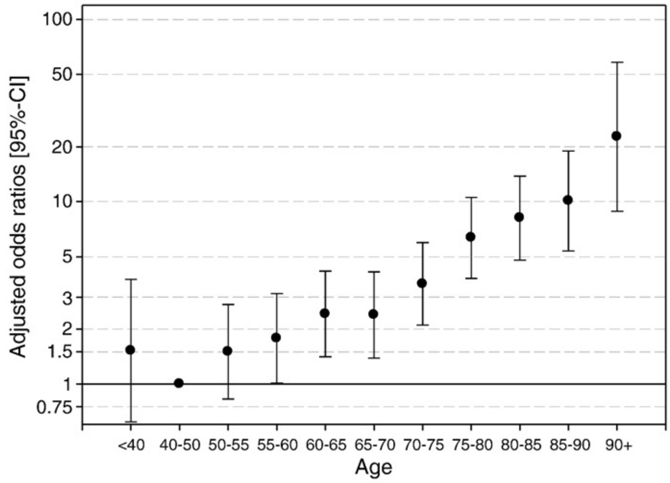

Fig. 2. Adjusted odds ratios of in-hospital mortality for different age groups.

3. Results

3.1. Baseline characteristics

For the present analysis patients were divided into four categories: ACS patients ≥75 ($n=4943$, 10.4%) and <75 years ($n=19{,}446$, 41.0%), and patients with stable angina ≥75 ($n=3393$, 7.2%) and <75 years ($n=19{,}625$, 41.4%). The baseline characteristics of the patients are shown in Table 1.

3.2. The angiographic and interventional characteristics

In the older group, coronary angiography revealed more severe CAD as compared with the younger patients. The elderly more often underwent PCI of left main stem and bypass grafts. There were no major age-related differences in the lesion characteristics. Drug-eluting stents were more often used in younger patients and in elective PCIs. Glycoprotein (GP) IIb/IIIa inhibitors were less frequently administered to older patients. Procedural success was high in young and old patients (Table 2).

3.3. Hospital complications

The incidence of hospital death was significantly higher in the elderly. This applies to patients undergoing PCI for stable CAD (0.5% versus 0.2%, $p<0.0001$) as well as for ACS (5.2% versus 1.7%, $p<0.0001$) (Fig. 1). Adjusted odds ratios of in-hospital mortality after revascularization procedures demonstrated a curvilinear relation with age, with a more rapid rise in patients older than 75 years (Fig. 2). The rate of non-fatal postprocedural myocardial infarction was higher in patients with ACS ($p<0.0001$), but there were no age-related differences. Among patients ≥75 years non-fatal strokes occurred more often in the setting of ACS ($p<0.001$). The incidence of major bleedings and renal failure requiring dialysis was significantly higher in older patients with ACS ($p<0.0001$, respectively) and stable angina ($p<0.05$, respectively) (Fig. 1).

3.4. Causes of death and discharge modes

The majority of patients died due to cardiovascular causes. On average, hospital survivors ≥75 years stayed longer in the treating interventional facilities and were more often discharged to other hospitals (Table 3).

3.5. Mortality predictors in patients ≥75 years with ACS

After adjustment for preprocedural, angiographic and interventional variables, multivariable logistic regression analysis revealed the following independent predictors of hospital mortality in decreasing order of importance (using odds ratios): haemodynamic instability, acute STEMI , acute segment closure, NSTEMI, TIMI <3 after PCI, chronic renal failure, history of stroke, left main disease, congestive heart failure, peripheral vascular disease, type C lesion, LAD stenosis, diabetes, female gender, 3-vessel disease and age (per 5-year increase) (Fig. 3).

3.6. Mortality predictors in patients ≥75 years undergoing elective PCI

The multiple logistic regression analysis demonstrated that the interventional index was the strongest predictor for death, followed by the preprocedural and angiographic index (Fig. 4).

4. Discussion

This analysis of the PCI-Registry of the Euro Heart Survey Programme with more than 47,000 patients including over 8000 patients ≥75 years gives a consistent overview of contemporary PCI practice. The data show that among this age group PCI can be performed with a relatively low rate of hospital complications. However, patients aged ≥75 years with coronary artery disease face a significantly higher risk for in-hospital death, mainly due to a higher prevalence of co-morbidities and a more severe degree of CAD.

There is neither a universal definition of nor accurate clinical criteria for the “elderly patient”. However, structural and functional changes of arteries are involved in the aging process [11,12]. These pathophysiological alterations and additionally the higher prevalence

Table 3
Hospital course: survival status, causes of death and discharge mode.

	ACS			Elective		
	Age ≥ 75 yrs. $n=4{,}943$	Age <75 yrs. $n=19{,}446$	*P*-value	Age ≥ 75 yrs. $n=3{,}393$	Age <75 yrs. $n=19{,}625$	*P*-value
Deceased patients	5.2%	1.7%	<0.0001	0.5%***	0.2%	<0.001
Length of stay post PCI [days]	2 (0–7)	2 (0–8)	ns	2 (0–17)	2 (0–5)	ns
Died on table	8.3%	17.4%	<0.05	0.0%	16.7%	ns
Cardiovascular causes	65.8%	63.0%	ns	60.0%	50.0%	ns
Cerebrovascular causes	2.5%	5.1%	<0.0001	0.0%	11.1%	ns
Non vascular causes	23.3%	14.5%	<0.0001	40.0%	22.2%	ns
Hospital survivors	94.8%	98.3%	<0.0001	99.5%***	99.8%	<0.001
Length of stay post PCI [days]	3 (1–6)	3 (1–5)	<0.0001	1 (1–2)	1 (1–2)	<0.0001
Discharge to home	73.1%	79.3%	<0.0001	91.0%***	93.9%	<0.0001
Discharge to other hospital	23.9%	18.7%	<0.0001	8.3%***	5.2%	<0.0001
Discharge to rehab-centre	3.0%	2.1%	<0.001	0.7%	0.9%	ns

*$P<0.05$ ≥75 yrs. ACS vs. ≥75 yrs. elective.
**$P<0.001$ ≥75 yrs. ACS vs. ≥75 yrs. elective.
***$P<0.0001$ ≥75 yrs. ACS vs. ≥75 yrs. elective.

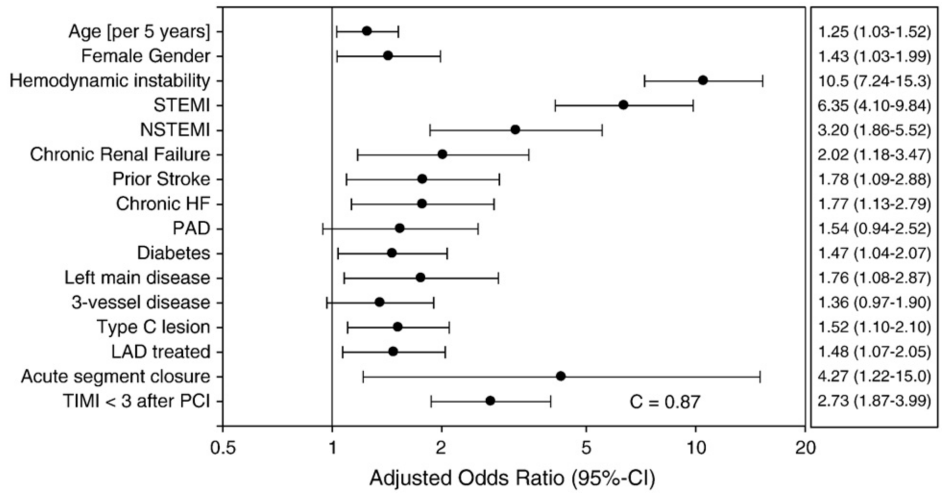

Fig. 3. Multiple logistic regression analysis of mortality predictors in patients ≥75 years with ACS (OR and 95% CI).

of cardiac and non-cardiac diseases contribute to the higher event rates among the elderly undergoing PCI. Although these physiological changes associated with aging do not appear at a specific age and do not proceed at the same pace in all individuals, most definitions of elderly are based on chronological age. In our study, a multiple regression analysis was conducted to determine the adjusted odds ratios of in-hospital mortality in different age groups. Periprocedural mortality risk after PCI demonstrated a curvilinear relation with age. An age cutoff of ≥75 years constituted an independent high-risk variable with a six-fold increased risk of in-hospital mortality. Thus, we chose to stratify the patients into two age groups – those <75 years of age and those 75 years and older – to highlight the differences between "elderly" and "nonelderly" patients.

PCI in the elderly carries a higher risk of acute coronary and other vascular complications. As stated above, age is clearly an independent risk factor for periprocedural mortality. However, the magnitude of risk depends strongly on the presence and severity of additional clinical, angiographic and procedural factors. Based on the large sample size, this analysis was able to determine a number of independent predictors of hospital mortality among patients ≥75 years with ACS. As expected, haemodynamic instability and acute STEMI were the strongest predictors of hospital death. Procedural variables were also strongly predictive of higher mortality in patients aged ≥75 years. In particular, both acute segment closure and TIMI flow <3 after PCI increased the risk of hospital death. Comorbidities such as history of stroke, congestive heart failure, chronic renal failure, peripheral artery disease and diabetes mellitus were also independent determinants of death. These findings are in line with prior studies investigating elderly patients undergoing PCI [8,9]. Even after adjustment for baseline, angiographic and interventional variables, female gender was associated with an increased mortality. This is of particular importance as women represent over 40% of all patients ≥75 years. Since women have smaller coronary vessels, it has been hypothesized that the worse outcomes are related to the mechanical factor of working in a smaller-diameter lumen [13]. Moreover, in an earlier study, Munoz also identified female gender as an independent predictor for major adverse cardiac events during a 3-year follow-up in the elderly [5]. In our study, the extent of coronary pathology determined the short-term outcome in patients ≥75 years. After adjustment, the presence of left main disease, LAD stenosis or 3-vessel disease was associated with a higher mortality. In addition, lesion characteristics seemed to play an important role; the presence of a type C lesion was predictive of hospital death.

Among patients aged ≥75 years undergoing elective PCI, clinical summary indices for preprocedural, angiographic and interventional information were constructed. Periprocedural complications were the strongest independent predictors of death. By contrast, in patients with ACS clinical instability was the most meaningful determinant for

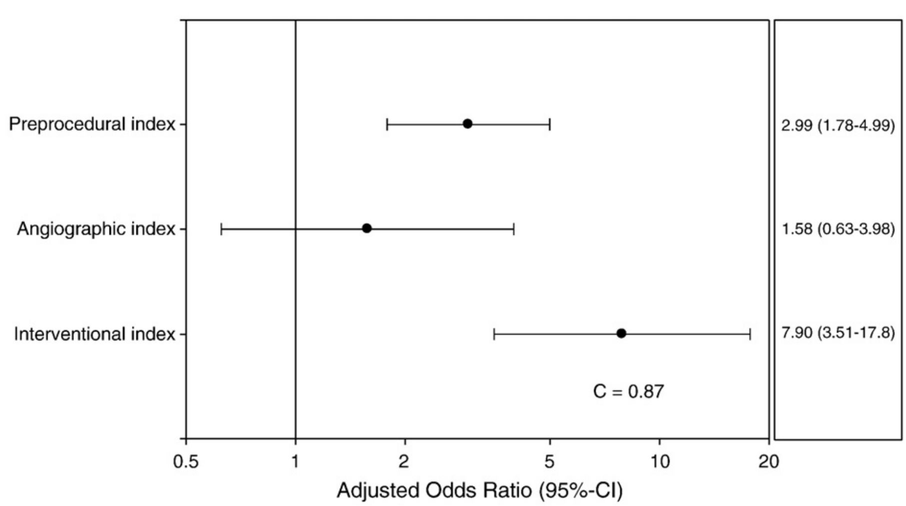

Fig. 4. Multiple logistic regression analysis of mortality predictors in patients ≥75 years undergoing elective PCI (OR and 95% CI).

hospital mortality. Furthermore, the preprocedural profile significantly affected the risk of death, whereas angiographic factors seemed to be less important. However, considering the low rate of adverse events these results need to be interpreted cautiously.

Despite this high risk profile among patients ≥75 years undergoing PCI was fairly low in our analysis. The presence of ACS substantially increases the rate of adverse events. After elective PCI the incidence of in-hospital death was only 0.5%, whereas 5.2% of the elderly with ACS died during the hospital stay. Nevertheless, compared with prior registry data, these are the lowest event rates ever documented in clinical practice. In the era predating stenting procedural mortality was almost 20% [14,15]. At the end of the 1990s, Munoz observed an in-hospital mortality of 2.3%, and Assali 6.6% after elective interventions in a period when the use of stents was still rather low [5,16]. More recently, data from a large North-American registry indicated a further reduction of peri-interventional complications with a death rate of 1.1% after elective and 11.5% after emergency PCI. Admittedly, these patients were older than 80 years [8].

Clinicians' reluctance to use an invasive treatment on the elderly has also been potentially justified by the high risk of non-cardiac complications. In our study the incidence of stroke, major bleeding episodes and renal failure requiring dialysis was significantly higher among patients ≥75 years. Nevertheless, compared with previous registry data there has been a further decrease in the rate of complications [8,9] despite the increasing risk profile of patients ≥75 years.

The relatively low rate of adverse events among the older group might be due to advances in PCI-technique, operator ability as well as adjunctive medical treatment. The procedural success was very good with no relevant residual stenosis in 94% of patients and TIMI 3 flow after PCI in over 93% of all treated lesions. Major age-related differences were not observed. In two prior studies assessing interventional results angiographic success was similar although only elderly patients receiving stenting were enrolled and the percentage of emergency PCI was significantly lower. In our analysis, more than 40% of the patients ≥75 years undergoing PCI received drug-eluting stents (DES). In a recent publication by Douglas et al., patients ≥65 years receiving DES had significantly better clinical outcomes than their counterparts treated with bare-metal stents [17]. The rate of adjunctive antithrombotic therapy in the older group was high, reflecting a good adherence to current practice guidelines, and no age bias [18]. Before or during PCI, almost 80% of the patients received dual antiplatelet therapy. The registry did identify a relatively low use of GP IIb/IIIa antagonists, with a selection bias towards patients with more complex interventions and a higher coronary thrombus burden. Among patients ≥75 years undergoing PCI for ACS only 27% received GP IIb/IIIa receptor blockers.

5. Limitations

The present analysis is not a randomized, controlled study. In the EHS PCI registry the treatment was left to the discretion of the physician. This may lead to a bias in the estimation of treatment effects, which cannot be fully eliminated even by using a multivariate analysis. Only patients undergoing PCI were enrolled into the registry which might reflect a selection bias towards the more fit elderly which had been considered for interventional treatment by the treating physician.

The EHS PCI registry was designed to document hospital course. No routine 30-day follow-up was planned. Therefore comparison of the hospital outcome of the elderly with younger patients might be difficult due to the differences in length of hospital stay. In survivors, the longer hospital stay in the elderly population reflects current clinical practice in the interventional treatment of coronary disease and is probably due to the higher prevalence of co-morbidities in the elderly.

6. Conclusions

The risk of adverse events among patients ≥75 years undergoing PCI is relatively low. This is probably due to advances in PCI-technique, operator ability and guideline-adherent adjunctive medical treatment. Nevertheless, complication rate is significantly higher than in younger patients. Among patients ≥75 years with ACS the most meaningful mortality predictors were haemodynamic instability and acute STEMI, followed by acute segment closure. Co-morbidities and severe coronary pathology also increased the risk for death. Interventional complications were the strongest determinants of hospital mortality among patients aged ≥75 years undergoing elective PCI. These observations imply a highly complex relationship among age, clinical, and procedural factors, and prognosis that will require further investigation.

Acknowledgement

The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [19].

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