ORIGINAL ARTICLE

Percutaneous Coronary Intervention in Octogenarian Patients: Long-term Outcomes and Predictors of Adverse Outcome

Angioplastia coronaria en pacientes octogenarios. Resultados alejados y predictores de mal pronóstico

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ABSTRACT

Background: Coronary percutaneous intervention in octogenarian patients is growing due to the rise in life expectancy. However, this population is underrepresented in randomized trials due to its high risk.
Objectives: The aim of this study was to evaluate short and long-term outcomes of coronary percutaneous intervention in octogenarian patients, and to identify independent predictors of adverse outcome.
Methods: This was a retrospective study including consecutive patients undergoing percutaneous coronary intervention at a general hospital from June 2011 to September 2013. Octogenarian patients (age ≥80 years) were compared with younger patients. Medical history, procedure characteristics and clinical outcomes were evaluated. Major adverse cardiovascular events (MACE consisting of death, myocardial infarction or stroke) were evaluated at 1 month, and 1 and 3 years. Multivariate analysis was performed to assess independent predictors of adverse outcome.
Results: A total of 1,030 patients (20.2% octogenarians) were included in the study. Mean age of octogenarian patients was 83 years (IQR 81-86). This population had more cardiovascular risk factors and comorbidities. No differences were observed in procedure success and number of implanted stents. The rate of MACE was significantly higher in octogenarian patients at 1 month (14.4% vs. 4.9%; p<0.001), 1 year (23.9% vs. 8.5%; p<0.001) and 3 years (p<0.0001), due to increased mortality, without differences in myocardial infarction (4.8% vs. 3.8%), stroke (1.7% vs. 1.6%), or procedural complications. Independent predictors of mortality in octogenarian patients were kidney failure, chronic obstructive pulmonary disease and ventricular dysfunction. Age ≥80 years was an independent predictor of MACE in the overall population.
Conclusions: Technical success was acceptable in octogenarian patients undergoing percutaneous coronary intervention, but octogenarian patients showed increased early and long-term mortality that appears to be independent of the procedure. Kidney failure, chronic obstructive pulmonary disease and ventricular function impairment were independent predictors of adverse outcome in these patients.

Key words: Aged, 80 and over – Angioplasty /Mortality - Angioplasty /complications – Comorbidity

RESUMEN

Introducción: La angioplastia coronaria en octogenarios aumenta, pero esta población está poco representada en los estudios aleatorizados por su alto riesgo.
Objetivos: Evaluar los resultados de angioplastia coronaria de pacientes octogenarios e identificar predictores independientes de mala evolución en el seguimiento.
Material y métodos: Estudio retrospectivo, pacientes consecutivos con angioplastia coronaria junio 2011 a Septiembre 2013 en un Hospital Polivalente. Se compararon octogenarios (edad ≥80 años) con el resto. Se evaluaron las características basales y del procedimiento. Se evaluó la mortalidad y los eventos cardiovasculares mayores (MACE, muerte, infarto o stroke) a 30 días, 1 y 3 años. Se realizó un análisis univariado y multivariado para predictores de mala evolución.
Resultados: Se incluyeron 1030 pacientes, 20,2% octogenarios. La edad promedio de los octogenarios era de 83 años (RIC 81-86). Estos presentaron más factores de riesgo y comorbilidades. La tasa de éxito y la cantidad de endoprótesis fue similar entre los grupos. La tasa de MACE fue mayor en octogenarios a 30 días (14,4% vs. 4,9%; p <0,001), 1 año (23,9% vs. 8,5%; p <0,001) y a 3 años (p <0,0001), a expensas de mortalidad sin diferencias en el infarto (4,8% vs. 3,8%), el stroke (1,7% vs. 1,6%), ni en complicaciones del procedimiento. Los predictores independientes de muerte en octogenarios incluyen IRC, EPOC y deterioro de la función ventricular. La edad ≥80 años fue un predictor independiente de MACE en la población general.
Conclusiones: Observamos una aceptable tasa de éxito de angioplastia coronaria en pacientes octogenarios, asociada con un aumento de la mortalidad inmediata y alejada que no parece relacionada con el procedimiento. La IRC, el EPOC y el deterioro de la función ventricular son predictores independientes de mal pronóstico en estos pacientes.

Palabras clave: Anciano de 80 o más Años – Angioplastia Coronaria/ mortalidad - Angioplastia Coronaria/complicaciones – Comorbilidad

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Abbreviations

COPD	Chronic obstructive pulmonary disease	**KF**	Kidney failure
HTN	Hypertension	**MACE**	Major adverse cardiovascular events

INTRODUCTION

The population of octogenarian patients (age ≥80 years) is steadily growing due to the rise in life expectancy. (1) The high prevalence of coronary artery disease in this group of patients, together with the continuous development of endovascular treatment by percutaneous coronary intervention (PCI) have increased the use of this type of procedures in elderly patients. (2-5) Moreover, these patients are at greater risk for surgical revascularization, contributing to the increase of PCI in this population. Regardless of the age group, PCI safety and outcome has improved in the last years, partly due to the technological advances in stents and to technical changes, as radial artery access, associated to the development of new antithrombotic and antiplatelet agents. (6-8)

Despite octogenarian patients are an increasingly growing group in hemodynamic labs, there is limited data in the literature regarding current PCI efficacy and safety in this population, as they are excluded from large randomized clinical trials. (4) Age is one of the main reasons for their omission, probably due to their comorbidities as confounding factors for the interpretation of clinical treatment results. (9-12) The few data from this population thus come from small observational studies and some international registries from large centers, showing that octogenarian patients have higher mortality, especially those with other comorbidities or history of cardiovascular disease. In our setting, however, there are no data on PCI results in this population. Therefore, the aim of the present study was to evaluate short-term and long-term PCI outcomes in octogenarian patients and to identify independent predictors of adverse outcome during follow-up.

METHODS

Population and study design

This was a single center, retrospective, observational study, including all patients undergoing PCI between June 2011 and September 2013 at Hospital Italiano de Buenos Aires, a tertiary general hospital in the Autonomous City of Buenos Aires.

Baseline characteristics, risk factors and cardiovascular history data was collected from the clinical records of each patient as well as the clinical condition for PCI indication, type of procedure, type of stent and medication used during the procedure.

Endpoints

The primary endpoint was 30-day mortality. Secondary endpoints were: 1) mortality at 1 year; 2) the combined endpoint (MACE) of acute myocardial infarction (AMI), stroke and 30-day and 1-year mortality; 3) each MACE endpoint separately; 4) vascular access complications; 5) stent acute thrombosis; 6) major bleeding; and 7) need for transfusion at 30 days of the procedure.

Variables

The last ventricular function study by either echocardiography, myocardial perfusion study, magnetic resonance imaging or computed tomography angiography, performed up to one month before PCI, was considered. Ejection fraction ≤35% defined severe ventricular function impairment. Urgent procedure was considered as that needing treatment within 24 hours of case presentation, and emergency when it was performed as quickly as possible within 120 minutes of its requirement. Other procedures were considered elective, i.e. they were programmed, without the patient being hospitalized. All-cause mortality was evaluated. Acute myocardial infarction was defined according to its third definition (10) and stroke was identified as any focal neurologic deficit (including coma) associated to a compatible brain image (computed tomography scan or magnetic resonance imaging). A procedure was considered successful when the percent residual stenosis after PCI was below 20%. Cardiogenic shock was defined as vasoactive drug or intraaortic balloon counterpulsation requirement due to sustained hypotension despite volume expansion with crystalloids. Vascular complications included: vessel occlusion at the level of the puncture site; large hematoma at the puncture site prolonging hospital stay; pseudoaneurysm documented by color Doppler echography; puncture site bleeding requiring transfusions or surgical repair; iliac or femoral artery dissection; or acute ischemia of the access limb. Major bleeding was defined as that fulfilling the following criteria: 1) fatal bleeding; 2) intracranial bleeding; 3) bleeding requiring transfusion of ≥4 IU of red blood cells. Acute stent thrombosis included both definite and probable thrombosis, defined as suspicious sudden death without apparent cause within 30 days of the procedure or confirmed by angiography.

Statistical analysis

Continuous variables with non-normal distribution were expressed as median and interquartile range and compared using the Mann-Whitney test for unpaired samples. Categorical variables were expressed as percentages and compared with the chi-square test and eventually Fisher´s exact test. Kaplan Meier survival and event-free survival curves were performed and compared with the Log-Rank test. Finally, univariate analysis of baseline characteristics was made and those variables with $p < 0.1$ entered a multivariate analysis. Statistical significance was defined as $p < 0.05$. The "R" statistical program (Auckland, New Zeland) was used to analyze the data.

Ethical considerations

The study was approved by the institutional Ethics Committee for Research Protocols in accordance with the 1975 declaration of Helsinki principles, amended in 1983 and reviewed in 1989.

RESULTS

A total of 1,030 patients (20.2% octogenarians) were included in the study. Complete data collection was

achieved in 97% of cases at 1-year follow-up. Figure 1 shows baseline characteristics. The group of octogenarian patients exhibited greater proportion of men and more prevalence of cardiovascular risk factors as chronic kidney failure (KF), hypertension (HTN), smoking and chronic obstructive pulmonary disease (COPD). They also had more frequent history of cerebral and peripheral vascular disease, but without differences in history of coronary heart disease. Octogenarian patients presented more often as acute coronary syndromes (ACS), though without difference in the rate of ST-segment elevation ACS (STEACS) and showed greater incidence of severe ventricular function impairment prior to PCI. They also presented with greater frequency complex disorders such as cardiogenic shock. Conversely, patients <80 years presented more often with stable conditions and the procedures were mostly programmed. Success rate for PCI was close to 93% for both groups and at least 1 stent was implanted in 95.4% of patients, with no differences between groups. Although there were no differences in the number of stents per patient, patients ≥80 years had longer procedures, drug-eluting stents (DES) were less often used, bivalirudin was more frequently administered as anticoagulant agent and glycoprotein IIbIIIa inhibitors were less frequently utilized (Table 1).

The rate of MACE at early (30 days) and long-term (1 year) follow-up was significantly higher in octogenarian patients (Tables 2), due to increased mortality, but without differences in the rate of AMI or stroke. Neither were there significant differences encountered in the need for revascularization of the treated vessel (6.2% in ≥80 years vs. 7.9% in <80 years, p=ns), stent thrombosis (1.4% in ≥80 years vs. 0.9% in <80 years, p=ns), nor vascular complications at the puncture site (0.5% in ≥80 years vs. 1.2% in <80 years, p=ns). Despite presenting similar rates of AMI and revascularization during follow-up, octogenarian patients had more readmissions for cardiovascular causes at one year (29.7% vs. 21.9%, p<0.05), and longer average hospital stay after PCI (5.6 vs. 3.6 days, p<0.01). Furthermore, the need for transfusions after PCI (at 30 days) was higher in octogenarian patients (5.7% in ≥80 years vs. 1.2% in <80 years, p<0.001) though without significant difference in the rate of major bleeding (1.9% in ≥80 years vs. 0% in <80 years, p=ns). The survival curve (Figure 1) was obtained from 94% of patients with very long-term data (above 3 years), confirming the results of significantly increased mortality in octogenarian patients.

In the univariate analysis, the characteristics associated with higher mortality in the group of octogenarian patients during follow-up were chronic KF (expressed as creatinine >1.5 mg/dl or dialysis requirement), history of COPD, presentation as ACS and severe ventricular function impairment. However, in the univariate analysis, chronic KF (with both measurements), COPD and severe left ventricular dysfunction were independent predictors of mortality (Table 3), the latter presenting the strongest association level.

Finally, age ≥80 years was an independent predictor of MACE at 1 year in the multivariate analysis (2.01 95% CI 1.27-3.18, p<0.01) after adjusting for risk factors (severe ventricular dysfunction, KF, ACS, peripheral vascular disease (PVD), female gender, COPD, HTN and previous stroke).

DISCUSSION

Octogenarian patients are a growing group of patients in the hemodynamic lab receiving revascularization strategies. (2, 3) In addition to a high index of comorbidities, they exhibit changes associated with ageing of vascular structures, including media calcification, diffuse atherosclerotic disease, dilation (positive remodeling), tortuosity and higher involvement of endothelial function. (3) All these changes contribute in defining octogenarian patients as a special population that deserves to be studied in detail. However, this group of patients is scarcely represented in clinical trials, and even less reported in our setting,

Despite the existence of ageing changes in atherosclerotic disease, our study did not find greater technical complexity in these patients, with a similar PCI success rate and the same number of stents implanted. Only the procedure time was longer in this group, which might probably reflect longer time to prepare (predilate) the lesion due to possible calcification, longer time to position the stent due to tortuous vessels and/or greater need of post-dilation. However, these variables were not assessed in this study.

As previously reported, octogenarian patients represent a group at greater risk, as they present more cardiovascular risk factors, more prior history of cardiovascular disease (stroke, cardiomyopathy, PVD, etc.) and more often present with acute disorders. Hence, mortality and rate of MACE in this group was higher. However, this increase in mortality does not seem to be associated with the procedure or the coronary heart disease, as there were no differences in the rate of infarction or stent thrombosis/restenosis. It might be speculated that frailty and age-related comorbidities might reflect the high mortality of our series, reflected by an increase in "non-coronary" cardiologic hospitalizations, probably corresponding to arrhythmias and/or heart failure. In agreement with this hypothesis, age ≥80 years was a predictor of MACE at follow-up, independently of these comorbidities, in accordance with other registries with a higher number of patients. (14-15)

On the other hand, different from other studies, (6-8) no differences were found in the rate of complications at the puncture site. Several reasons could explain this result, as radial access, (16) use of bivalirudin, skill of the operators or the measurement device, but an increase in need for transfusions and longer hospital stay was observed.

	Total (n=1,030)	<80 years (n=821)	≥80 years (n=209)	p
Baseline characteristics				
Male gender	72.4%	77.2%	53.6%	<0.0001
Age (years)	68 (60-77)	65 (58-72)	83 (81-86)	<0.001
Baseline Cr. (mg/dl)	1.02 (0.85-1.2)	0.99 (0.83-1.1)	1.12 (0.93-1.35)	<0.0001
Cr. >1.5 mg/dl	9.7%	7.7%	17.7%	<0.0001
Diabetes	19.4%	20.2	16.3	NS
HTN	79.1%	75.5%	93.3	<0.0001
Smoking	57.2%	62%	38.3%	<0.0001
COPD	6.2%	5.4%	9.6%	<0.05
Dyslipidemia	64.7%	66%	59.3%	NS
Dialysis	2.7%	2.4%	3.8%	NS
Previous AMI	24.8%	23.8%	28.7%	NS
Previous PCI	30.6%	31.3%	27.8%	NS
Previous CABG	9.6%	9%	12%	NS
Previous stroke	3.9%	2.9%	7.7%	<0.01
PVD	11.9%	8.9%	23.9%	<0.0001
Severe LVSF impairment	7.5%	6.3%	12.5%	<0.01
Clinical presentation				
CSA	39.1%	41.8%	28.7%	<0.001
NSTEACS	39.6%	37.6%	47.4%	<0.01
STEACS	20.9%	20.2%	23.4%	NS
Cardiogenic shock	6.8%	5.7%	11%	<0.01
Procedure characteristics				
Programmed	39%	41%	28%	<0.001
Urgency	36%	33%	45%	<0.01
Emergency	24.7%	23.2%	26.3%	NS
PCI success	93.1%	93.2%	92.8%	NS
Number of stents	1.68	1.7	1.62	NS
Use of DES	63.1%	66%	51.7%	<0.001
Multivessel PCI	20.9%	20.6%	22%	NS
Fluoroscopy time (min)	20.2 (14-30.4)	19.4 (13.2-29.8)	23.5 (16.5-32.6)	<0.001
Use of bivalirudin	15.1%	12.7%	24.5%	<0.001
Use of IIbIIIa	9.6%	11%	3.8%	<0.01

Table 1. Baseline and procedure characteristics

Cr.: creatinine. NS: Not significant. HTN: Hypertension. IAM: Acute myocardial infarction. PCI: Percutaneous coronary intervention. CABG: Coronary artery bypass grafting. PVD: Peripheral vascular disease. LVSF: Left ventricular systolic function. COPD: Chronic obstructive pulmonary disease. CSA: Chronic stable angina. NSTEACS: Non-ST-segment elevation acute coronary syndrome. STEACS: ST-segment elevation acute coronary syndrome. DES: Drug-eluting stent. IIbIIIa: Glycoprotein IIbIIIa inhibitors.

In the multivariate analysis three independent predictors of mortality were found in octogenarian patients: KF, ventricular dysfunction and COPD. Since these comorbidities are not infrequent in this population, and that some patients may present more than one, a previous correct evaluation is recommended (anamnesis, laboratory tests and echocardiogram), whenever possible, to identify groups at greater risk. Moreover, in some situations and considering the advanced age of this population, the need for PCI should be balanced with the patient's risk and life expectancy.

In this study bivalirudin was used as anticoagulant agent in 1 out of 4 elderly patients. Probably, this does not represent our current practice, since several recent studies have been unable to clearly demonstrate the superiority of bivalirudin over heparin, at the expense of a potential increase of the rate of stent thrombosis. (17) However, these studies were published after 2013.

The present study has several limitations, despite

Table 2. Early and long-term cardiovascular events in octogenarian patients

	Total (n=1,030)	<80 years (n=821)	≥80 years (n=209)	p
MACE at 30 days	6.8%	4.9%	14.4%	<0.0001
Death at 30 days	4.9%	2.9%	12.4%	<0.0001
AMI at 30 days	1.6%	1.5%	1.9%	NS
Stroke at 30 days	0.9%	0.9%	1%	NS
MACE at 1 year	11.7%	8.5%	23.9%	<0.0001
Death at 1 year	7.7%	3.9%	22.5%	<0.0001
AMI at 1 year	4%	3.8%	4.8%	NS
Stroke at 1 year	1.7%	1.6%	1.9%	NS

MACE: Major adverse cardiovascular events (death, AMI or stroke). AMI: Acute myocardial infarction. NS: Not significant.

Fig. 1. Kaplan-Meier combined event-free survival curves of patients >80 and <80 years.

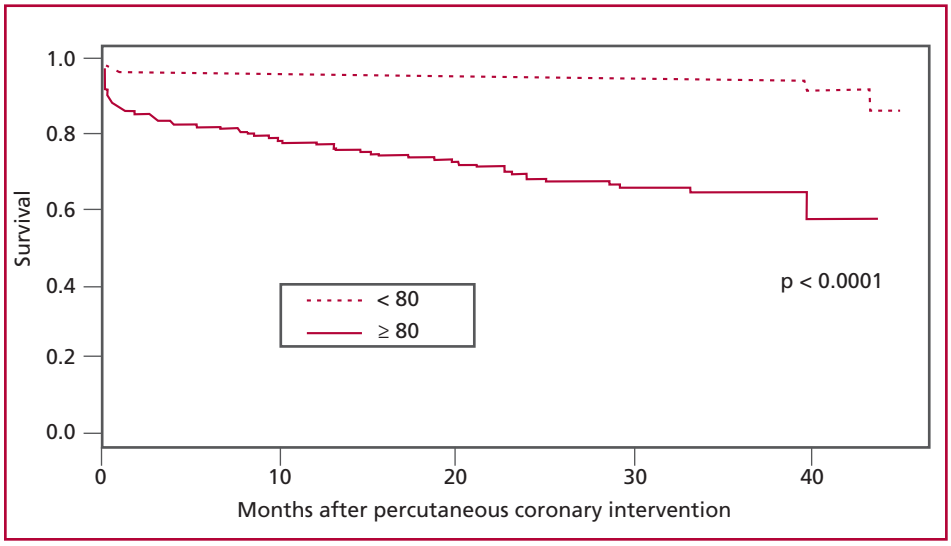

Table 3. Multivariate analysis of mortality during follow-up in octogenian patients

	OR (CI95)	p
Severe LVSF impairment	2.76 (1.55 a 4.90)	<0.001
Creatinine ≥1.5 mg/dl	2.38 (1.34 a 4.25)	<0.01
Dialysis	2.74 (1.07 a 7.01)	<0.05
COPD	2.19 (1.15 a 4.18)	<0.05

LVSF: Left ventricular systolic function. COPD: Chronic obstructive pulmonary disease.

the importance of the results. First, it is a single center, retrospective study in a general hospital of the Autonomous City of Buenos Aires. Second, as previously stated, some anatomical variables of the procedure (calcification, tortuosity, lesion length) were not measured, precluding the detailed anatomical complexity of the procedure. Third, multiple logistic regression analysis was performed to compare between groups, without using a propensity score. However, epidemiological studies did not find differences between both methods. (18, 19) Finally, the present study only included patients undergoing PCI, so caution should be exercised when generalizing the results, as patients not considered candidates for coronary angiography and those in whom coronary angiography was performed but not PCI because medical treatment or coronary bypass grafting was decided, were excluded from the study.

CONCLUSIONS

Percutaneous coronary intervention in octogenarian patients seems to be an acceptable and safe procedure with a high rate of success and low risk of complications. Mortality in this group is high due to greater prevalence of comorbidities, among which, KF, ventricular function impairment and COPD are independent predictors. Age ≥80 years represents a predictor of adverse outcome independently of comorbidities.

Conflicts of interest

None declared. (See authors' conflicts of interest forms on the website/Supplementary material).

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