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Original article

Evaluation of the impact of chronic kidney disease on the survival of octogenarian patients submitted to percutaneous coronary intervention

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ABSTRACT

Objective: To evaluate the impact of chronic kidney disease on the survival of patients – 80 years of age undergoing percutaneous coronary intervention (PCI) in the long term.
Methods: 273 subjects who underwent PCI between January 2010 and January 2016 were divided into four categories: (1) stable angina (SA) and creatinine clearance – 30 (n = 24); (2) patients with SA and CrCl <30 (n = 70); (3) patients with acute coronary syndrome (ACS) and CrCl – 30 (n = 51); (4) patients with ACS and ICC <30 (n = 128). Mortality curves were evaluated using the Kaplan-Meier method and differences between groups were compared by log-rank statistic. Multivariate analysis was performed using the Cox proportional hazards method. The 4 groups were compared and the survival between the groups was evaluated.
Results: Octogenarian patients with CrCl <30 with SA and ACS have lower long-term survival ($p < 0.0001$).
Conclusion: CKD has a worse long-term prognosis for patients undergoing PCI.

1. Introduction

Coronary artery disease (CAD) is the leading cause of death in patients with chronic kidney disease (CKD).[1,2] In these patients, increased mortality is explained by a higher prevalence of cardiovascular risk factors, such as hypertension, diabetes mellitus (DM), dyslipidemia and uremia, which promote rapid progression of CKD.[3]

Patients with CKD have a high risk of adverse clinical outcomes following coronary artery bypass grafting (CABG), including a higher incidence of acute myocardial infarction (AMI), compared to non-CKD patients.[4] In a larger study, in-hospital mortality factors after percutaneous coronary intervention (PCI) in more than 25,000 patients, CKD, especially end-stage CKD, is independently associated with increased mortality. Independent risk factors in patients with CKD included myocardial infarction within 72 h, while PCI was associated with increased risk of death in patients with moderate CKD.[5]

Although PCI may be a high-risk procedure in CKD, PCI has been associated with a lower risk of death in patients with CKD, when compared to non-percutaneous revascularization.[6] Thus, the presence of renal disease or dialysis dependence should not preclude percutaneous revascularization in patients with acute coronary syndrome (ACS). PCI has been associated with a lower risk of death in patients with CKD, when compared to non-percutaneous revascularization. Thus, if CAD is highly suspected in dialysis patients, invasive procedures such as coronary angiography and coronary revascularization should be performed. However, despite the prevalence of studies reporting an adverse association of CKD and PCI in ACS, there is still a lack of studies on the actual impact of CKD on the initial results of elective PCI.

In elderly patients, the incidence of ischemic heart disease (IHD) and the need for PCI have also increased.[7] In patients ≥75 years, 40% of deaths are caused by IHD. In addition, age is closely related to higher mortality and the incidence of post-PCI complications.[8,9] Although age itself is not a contraindication to PCI, there is a lack of data on the best management of elderly patients undergoing PCI. Thus, safety and efficacy of PCI should be assessed for this specific group.

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The objective of this research is to evaluate the impact of stage 4 and 5 CKD in 80-year-old patients undergoing coronary angioplasty.

2. Methods

We retrospectively analyzed 4810 patients who underwent angioplasty at the Invasive Cardiology and Hemodynamics service at the Hospital de Base in São José do Rio Preto from January 2010 to January 2016. The follow-up included data on mortality and complications obtained by reviewing medical charts and recent visits to the outpatient clinic or telephone contacts for a minimum period of 1 year after the procedure. Of this total, 336 patients were ≥ 80 years of age. Data was collected for age, weight, height, risk factors, procedure time, creatinine, percutaneous access route, clinical condition, ethnicity, treated coronary artery and type of stent used. Of the total number of octogenarians, 3 were excluded because they had dialytic chronic renal failure, 8 due to angioplasty failure, 30 because they had cardiogenic shock at the moment of hospital admission, and 22 were lost to follow-up. Serum creatinine was determined 0–6 hours prior to PCI and creatinine clearance (CrCl) was estimated using the Cockroft-Gault formula: CrCl (ml / min) = [(140-age) × weight (kg)] (mg / dL) (×1 for men, ×0.85 for women) and the MDRD formula: 186.3 × (creatinine mg / dL) $^{-1154}$ × age$^{-0.203}$ × (0.742 if female) × 1.21 if black). We established the cut-off point at 30 ml/min of CrCl and assessed survival matched by clinical condition: stable angina and ≥30 or <30 and clearance of patients with ACS (unstable angina, non-myocardial acute myocardial infarction ST segment and above ST segment) to evaluate survival. The primary objective was to assess mortality from all causes. Data analysis was performed by SPSS Statistics 22.0 (IBM Corporation, Somert, NY) and Project R 3.2.1. Differences between groups were compared by Student's *t*-test for continuous variables and Chi-square or Fisher Exact for tests with dichotomous variables. A value of $p \leq 0.05$ was considered significant. Mortality curves were evaluated using the Kaplan-Meier method and differences between groups were compared by log-rank statistic. Multivariate analysis using the Cox proportional hazards method was constructed. The selected variables were first-tested for significance (defined as $p < 0.2$). The variables considered significant were then included in the multivariate logistic regression analysis using stepwise selection. The study protocol was approved by the research ethics committee, São José do Rio Preto School of Medicine, FAMERP under the number 63,700,917.2.0000.5415.

3. Results

This study evaluated 4810 patients of which 336 (7.0%) were ≥ 80 years of age. Sixty-three patients did not meet the inclusion criteria (Fig. 1). Therefore, 273 patients ≥ 80 years of age were fully evaluated. Mean follow-up time was 72 months with a minimum of 12 months. The largest subgroup of patients was the one with CrCl≥30 and ACS (128/273; 46.9%). We observed that among patients with ClCr≥30, the age variable was significantly higher in the ACS group (83.4 ± 3.6 versus 81.7 ± 2.3; p = 0.0016) and there was also a larger number of smokers in this group (4.3% versus 15.6%; p = 0.0146), whereas the opposite was observed for BMI (25.8 ± 3.9 versus 27.1 ± 4.3; p = 0.0263). Mortality was also higher in this group with high CrCl and ACS (33.6% versus 12.8%; p = 0.0012). In the subgroup of patients with CrCl<30, none of the study variables showed a statistically significant difference when cases of ACS and stable angina (SA) were compared, including survival at the end of 6 years of follow-up (68.6% versus 58.3%; p = 0.5258). We highlight that survival was significantly lower in the in-group comparison (ACS group with high CrCl vs ACS group

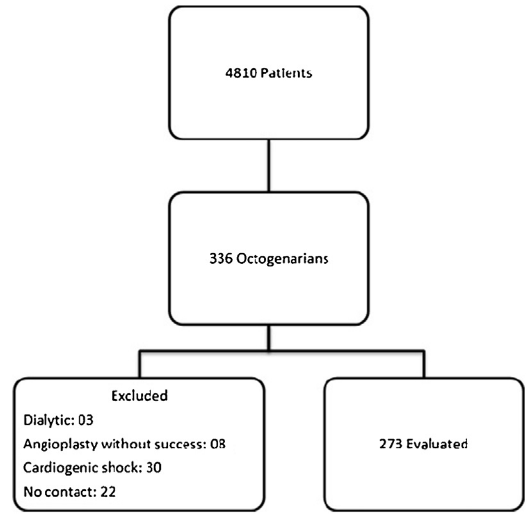

Fig. 1. Flow Chart showing the population of patients studied and excluded.

with low CrCl and SA group with high CrCl versus low CrCl) with p < 0.0001 in both combinations. This was valid for both forms of CrCl calculation (MDRD/Cockroft-Gault). A complete list of study results may be found in Table 1 and Figs. 2 and 3 illustrate the Kaplan-Meier survival curves.

4. Discussion

In our study, we evaluated all-cause mortality in 80-year-old patients with a minimum follow-up of 1 year, from January 2010 to January 2016. Among the cardiovascular risk factors, hypertension was observed in 84.98%, DM in 32.6%, active smoking in 11.35% and there were a total of 101 deaths in the follow-up. In graph 1, a scatter diagram demonstrates that the Cockcroft-Gault and MDRD formulas are excellent methods to evaluate renal function. Current literature does not make clear how to assess CrCl in very old patients, which sometimes leads to an additional difficulty in evaluating these patients.[9,10]

We did not identify the individual causes of death. However, based on a Swedish study indicating that the overall mortality in octogenarian patients hospitalized for ACS was around 46% over 5 years and in our study we observed a general mortality around 48% in the group with CrCl>30 in 2500 days.[10] We observed that female gender and age were independent predictors of increased mortality in the ACS group. Previous studies have pointed to the association of the female gender with a worse prognosis, both in ACS or SA treated by PCI, as well as anterior interventricular coronary angioplasty as a predictor of increased mortality.[11,13,14] but this was not observed in the study.

Patients with SA and CrCl ≥30 presented a better prognosis and patients with ACS and CrCl <30 presented worse prognosis (charts 2 and 3). We also assessed that CrCl < 30 has a worse prognosis than the clinical condition of ACS. A study by Chen et al in patients ≥75 years evaluated that CKD had a worse prognosis in patients submitted to coronary angioplasty due to SA and ACS involving CKD as a risk factor for elderly patients undergoing PCI.[12] Considering the evaluation of general data we found that among the risk factors evaluated, smoking was statistically significant among patients with ACS and ACS with CrCl ≥ 30. Previous studies have evidenced this association and also corroborate that hypertension and DM did not have an impact on survival.[12–14]

When analyzing Figs. 2 and 3, we observed the sharp increase in mortality in both patients who presented with SA and in the presence of ACS when in the 4 and 5 stages of CKD. These data are

Table 1
Baseline clinical characteristics by treatment modality and renal function. CrCl, Creatinine clearance; SA, stable angina; ACS, acute coronary syndrome; BMI, body mass index; DM, diabetes mellitus; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; RIn, ramus intermedius artery; LCT, left coronary trunk ; LCX, left circumflex coronary artery; RCA, right coronary artery.

Parameters/ClCr	<30		intra	≥30		intra	intra inter-AS	inter ACS
Clinical condition	SA (24)	ACS (51)	valor-P	SA (70)	ACS (128)	valor-P	valor-P	valor-P
Age	86.1 ± 4,4	84.3 ± 4,7	0.1143	81.7 ± 2,3	83.4 ± 3,6	0.002	<0.0001	0.5190
Gender (male)	10	15	0.3100	40	69	0.666	0.2021	0.0031
BMI	23.6 ± 2.9	24.3 ± 4.5	0.4510	27.1 ± 4.3	25.8 ± 3.9	0.026	0.0002	0.0365
Hypertension	21	46	0.7241	62	102	0.115	0.8648	0.0926
DM	4	19	0.0756	22	44	0.681	0.0756	0.7154
Smoking	1	7	0.2402	3	20	0.015	>0.9999	0.7707
Procedure time	43.6 ± 15,2	45.8 ± 23,6	0.8198	50.4 ± 21.4	43.7 ± 20.2	0.025	0.2217	0.5742
Radial Access	16	32	0,7554	53	76	0,021	0,4002	0,6849
Localization of angioplasty								
LAD	12	27	0.8170	40	65	0.397	0.5536	0.7975
LCX	5	16	0.3625	21	24	0.078	0.4061	0.0768
RCA	9	20	0.8956	18	39	0.488	0.2874	0.2691
RIn	0	0	NA	1	5	0.379	0.7447	0.1828
LCT	1	2	0.9300	1	3	0.728	0.5106	0.5820
Conventional stent	22	44	0.5462	60	117	0.229	0.4913	0.3197
Drug-Eluting stent	2	6	0.6995	12	12	0.122	0.3214	0.6284
Blacks	2	8	0.4190	3	13	0.154	0.4820	0.3145
Deaths	14	35	0.5258	9	43	0.001	<0.0001	<0.0001

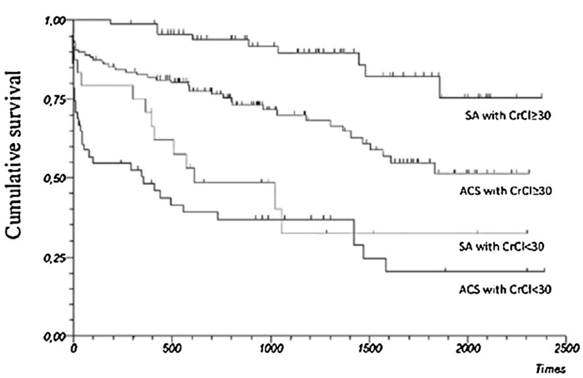

Fig. 2. ChartLong-term survival curves on stratified days by clicnical status (SA and ACS) and clearance creatinine admission. Clearance estimated by the Cockcroft-Gault formula. Curves generated using the Kaplan-Meier approach.

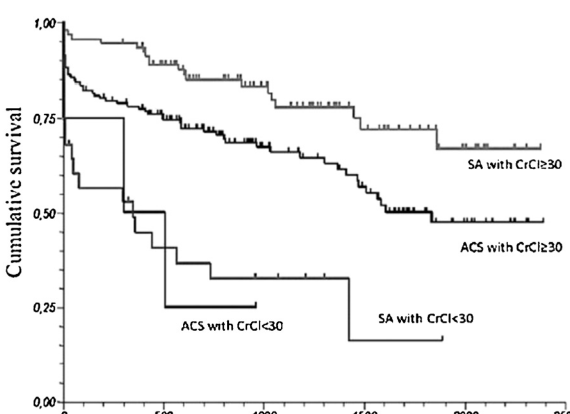

Fig. 3. Long-Term survival curves on stratified days by clinical status (SA and ACS) and clearance creatinine admission. Clearance estima\ted by the MDRD formula. Curves generated using the Kaplan-Meier approach.

consistent with previous reports evaluating the effect of CKD on cardiovascular disease.[15,17]

Other studies have also shown that the association between moderate to severe renal dysfunction and increased risk of death persisted after adjusting for initial imbalances among CKD groups, suggesting that alternative and independent mechanisms may be contributory in such patients. The excess risk may also be due to a systemic inflammatory state, stress and significant endothelial dysfunction, factors that may act synergistically to increase intracoronary thrombosis.[16,18,19]

Potential mechanisms by which CKD can increase the risk of acute stent thrombosis include increased propensity for thrombosis, increased systemic inflammation, glucose homeostasis disorders that may affect endothelialization patterns, and elevation of the hyperplastic response in an atherosclerosis environment with subsequent development of in-stent neoaterosclerosis.[18,20]

Patients with CKD have abnormal microvascular function even in the absence of coronary stenosis at angiography. Metabolic conditions are associated with increased stress, abnormal autonomic vascular tone regulation, changes in vascular smooth muscle reactivity and vasodilator response to hypoxia. The association of microvascular impairment after AMI with poor prognosis has been previously proven.[21–23]

Our population consisted of octogenarians, who are known to have a high incidence of comorbidities, in addition to more complex coronary lesions, calcified, thin and tortuous vessels than young patients. Hypertension, CKD, chronic obstructive pulmonary disease and peripheral vascular disease are more common among patients ≥75 years, which may imply a worse prognosis when revascularization is indicated.[24,26]

In our study, there was no difference in mortality between groups using drug-eluting stent (DES) and bare metal stent (BMS), favoring the idea of recent studies that point to this thesis, however, we emphasize that almost all of the previous studies did not evaluate the effect of stents in elderly patients, since they were excluded from the studies.[25,26]

One bias of this study was the low use of DES (<20%). If second generation DES are of choice in elderly patients undergoing PCI this has not yet been elucidated. Recent studies have demonstrated the superiority of second generation DES when compared to metal stents in patients over 75 years of age with SA and ACS or patients aged 80 years with SA to decrease the risk of thrombosis and in-stent stenosis.[26,27]

There was no increased mortality in association with traditional risk factors such as DM and hypertension. This may be due to the fact that DM is an important cause of CKD and it was already implicated in the increase of general mortality.[28]

5. Conclusion

In the evaluation of CKD in octogenarian patients undergoing PCI, we observed that impaired renal function reduces long-term survival and is the predominant clinical sign at admission (SA or ACS). We also observed that traditional risk factors, as well as the type of stent (BMS or DES) do not seem to impact survival over 7 years after angioplasty.

Conflict of Interests

All authors have no conflict of interests to declare.

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