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Emergency coronary angiography in a 90-plus population: outcomes at 5-year follow-up

Tânia Proença, Ricardo Alves Pinto, Miguel Martins Carvalho, Paula Dias, Filipe Macedo

Department of Cardiology, University Hospital Center of São João, Porto, Portugal

Abstract

Elderly people represent a vulnerable and increasing population presenting with acute coronary syndrome (ACS). Our goal was to evaluate a group of very old patients who underwent emergency coronary angiography (CA). We retrospectively analyzed a group of very old patients (≥90 years old) who underwent emergency CA from 2008 to 2020. Survival and major adverse cardiovascular events (MACE) (a composite of all-cause death, ischemic stroke, ACS, or hospitalization for acute heart failure) were compared with an aged-matched control population with ACS not submitted to emergency CA. A total of 34 patients were enrolled, 56% of whom were female, with a median age of 92 years old. Almost all patients had ST elevation-ACS. In CA, 65% had multivessel disease, and coronary intervention was performed in 71%. More than one-third evolved in Killip class III/IV, and 70% had left ventricular dysfunction. Regarding mortality, 38% of patients died in the index event *versus* 25% in the aged-matched control group (p=0.319). During 5 years of follow-up, there was no significant difference in mortality between the 2 groups (Log-rank=0.403) and more than 50% of patients died in 2 years. Comparing MACE occurrence, both groups were similar (Log-rank=0.662), with more than 80% having at least one event in 5 years. Very old patients submitted to emergency CA had a high rate of multivessel disease and left ventricular dysfunction, in-hospital and follow-up mortality, and MACE. Compared to an aged-matched control group not submitted to emergency CA, they showed no survival or MACE benefit during a 5-year follow-up.

Correspondence: Tânia Proença, Department of Cardiology, University Hospital Center of São João, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal.
E-mail: taniagproenca@hotmail.com

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Introduction

Ischemic heart disease represents the most common cause of death around the world, with higher mortality among older adults [1]. Elderly people represent a vulnerable and increasing population presenting with acute coronary syndrome (ACS), and even though advancing age is associated with poor outcomes, these patients tend to receive fewer evidence-based treatments, including coronary angiography [2,3]. Traditionally, older patients were underrepresented in ACS trials [4] and despite new contemporary trials, there is still a paucity of evidence comparing health outcomes [5].

Another issue is the definition of older age, since aging is a progressive condition without a universally accepted cut-off for older age [3]. As the aging population grows, especially in Western countries, more elderly patients will present to the emergency department with an ACS. It is no longer unusual to see nonagenarians admitted with ischemic heart events, which brings even more challenges to clinical practice. In the absence of robust data, European and American guidelines recommend weighing up the potential benefits against the risk of harm, accounting for frailty and cognitive status [2,6].

Considering the increasing 90-plus population, our study aimed to evaluate a group of very old patients who underwent emergency coronary angiography (CA).

Materials and Methods

We retrospectively analyzed a group of very old patients (≥90 years old) who underwent emergency CA from January 2008 to September 2020 at *Centro Hospitalar Universitario São João, E.P.E.*, a tertiary center in Porto, Portugal. A total of 34 patients were identified and enrolled in the study. Clinical features were collected at admission; the median follow-up in patients who survived the index event was 19 months [interquartile range (IQR) 6-54 months]. Major adverse cardiovascular events (MACE) were defined as a composite of all-cause death, ischemic stroke, ACS, or cardiovascular hospitalization for acute heart failure. Survival and MACE were compared with an aged-matched control population with ACS not submitted to emergency CA. Chronic kidney disease was defined as a baseline estimated glomerular filtration rate of less than 60 mL/min (Cockcroft-Gault equation). The degree of patients' disability or dependence in their daily activities was evaluated using the Modified Rankin Scale (mRS) [7]. This study was approved by the institutional ethics committee.

Data are presented as mean±standard deviation for paired continuous variables or median (IQR) for unpaired continuous variables and as numbers and percentages for categorical variables. A one-sample Kolmogorov-Smirnov test was performed to evaluate the normal distribution. Categorical variables were compared using the chi-square test. Time-to-event distributions were summarized with Kaplan-Meier curves, and groups were compared using Log-rank. For analyses of survival and MACE, data were censored at the time of loss to follow-up or on the closing date of the study. Differences were considered statistically significant when $p \leq 0.05$. Statistical analysis was performed in IBM SPSS Statistics version 25 (Armonk, NY, USA).

Results

We enrolled a total of 34 patients; 56% (n=19) were female, with a median age of 92 (91-93) years old. Baseline characteristics are summarized in Table 1. In respect to cardiovascular risk factors, 88% (n=30) had hypertension, 49% (n=16) had dyslipidemia, 12% (n=4) had diabetes, 15% (n=5) were smokers or previous smokers, and 15% (n=5) were obese. A total of 9 patients (27%) had a history of atrial fibrillation, and the median mRS score was 2 (slight disability).

Almost all patients had an ST-elevation myocardial infarction (STEMI), mostly located in the anterior wall in 68% of patients (n=23), followed by the inferior wall (21%, n=7); one patient had an infarction of indeterminate location. Emergency CA showed left main coronary (LMC) artery disease and multivessel disease in 9% (n=3) and 65% (n=22), respectively. The most frequent culprit was the left anterior descendent (LAD) artery (56%, n=19) followed by the right coronary artery (27%, n=11), LMC artery (9%, n=3), and circumflex artery (3%, n=1).

Primary coronary intervention (PCI) was performed in 71% (n=24) of patients (more than two-thirds with stent implantation), and the remaining patients maintained a conservative treatment. Differed PCI from non-culprit-artery was performed in 2 patients. At index-event admission, the median peak of high-sensitivity troponin I, brain natriuretic peptide, low-density lipoprotein cholesterol and hemoglobin (Hb) were respectively 131,517 (IQR 42,380-267,000) ng/L, 496 (IQR 331-1237) pg/mL, 163 (79.5-112.8) mg/dL and 11.4 (IQR 10.4-12.8) g/dL. During hospitalization, 36% (n=12) of patients evolved into Killip class III or IV and only 30% presented preserved left ventricular systolic function; in-hospital mortality was 38% (n=13). Of note, all patients whose culprit was LMC died in the index event.

Almost all patients were discharged on aspirin (95%, n=19) and the majority with dual antiplatelet therapy, clopidogrel in 70% (n=14), and ticagrelor in 10% (n=2) of patients. Only 2 (10%) were medicated with a direct oral anticoagulant due to concomitant atrial fibrillation, and none with warfarin. All patients were discharged on statin, mainly on statin of moderate intensity (60%, n=12). Inhibitors of the renin-angiotensin-aldosterone system (iRAAS) and b-blockers (BB) were prescribed in 65% (n=13) and 60% (n=12), respectively. More than half of the patients were discharged on loop diuretic, namely furosemide (60%, n=12) (Table 2).

Table 1. Baseline characteristics of study group.

N	34
Age, years, median (IQR)	92 (91-93)
Female, n (%)	19 (56)
Cardiovascular risk factors	
Hypertension, n (%)	30 (88)
Dyslipidemia, n (%)	16 (49)
Diabetes, n (%)	4 (12)
Smoker or previous smoker, n (%)	5 (15)
Atrial fibrillation, n (%)	9 (27)
Chronic kidney disease, n (%)	7 (21)
Previous cerebrovascular disease, n (%)	4 (12)
Modified Rankin Scale, median (IQR)	2 (0-3)
Acute event	
STEMI, n (%)	33 (97)
Anterior, n (%)	23 (68)
Inferior, n (%)	7 (21)
Infero-posterior, n (%)	2 (6)
Infero-lateral, n (%)	1 (3)
Infarction of indeterminate location, n (%)	1 (3)
Emergency CA	
Multivessel disease, n (%)	22 (65)
3-vessel disease, n (%)	8 (24)
2-vessel disease, n (%)	14 (41)
Left main disease, n (%)	3 (9)
Single-vessel disease, n (%)	12 (35)
Invasive treatment	
Primary coronary intervention, n (%)	24 (71)
Stent implantation, n (%)	17 (50)
Surgical revascularization, n (%)	0 (0)
Conservative treatment	10 (29)
High-sensitivity troponin I, ng/L, median (IQR)	131,517 (42,830-267,000)
Brain natriuretic peptide, pg/mL, median (IQR)	496 (331-1237)
Admission haemoglobin, g/dL, median (IQR)	11.4 (10.4-12.8)
Killip class	
I, n (%)	10 (30)
II, n (%)	11 (33)
III, n (%)	2 (6)
IV, n (%)	10 (30)
Left ventricle systolic function	
Preserved, n (%)	11 (32)
Mildly reduced, n (%)	6 (18)
Reduced, n (%)	17 (51)
In-hospital mortality	13 (38)

IQR, interquartile range; STEMI, ST-elevation myocardial infarction; CA, coronary angiography.

During follow-up, most patients developed signs and symptoms of heart failure, being at least in functional New York Heart Association class II (92%, n=12). On follow-up, the median value of Hb was 11 (IQR 10.0-12.6) g/dL.

Table 3 displays the baseline characteristics of the control group. When comparing the population in the study with the control group, 38% of patients died in the index event *versus* 25% in the aged-matched control group (p=0.319). During 5 years of follow-up, there was no significant difference in mortality between the two groups (Log-rank, p=0.403) and more than 50% of patients died in 2 years in both groups (Figure 1). Comparing MACE occurrence, both groups were similar (Log-rank, p=0,662), with more than 80% having at least one event in 5 years (Figure 2).

Discussion

New treatment strategies such as early coronary revascularization and optimized medical therapy profoundly changed the ACS prognosis. For patients younger than 75 years old, the superiority of invasive treatment is well documented from randomized evidence for both ST-elevation and non-ST-elevation-ACS [8]. More recently, some studies have evaluated the role of invasive treatment in older

Table 2. Medication prescribed at hospital discharge in the study group.

Antithrombotic, n (%)	20 (100)
Aspirin, n (%)	19 (95)
Clopidogrel, n (%)	14 (70)
Ticagrelor, n (%)	2 (10)
DOAC, n (%)	2 (10)
Warfarin, n (%)	0
Statin, n (%)	19 (95)
Low intensity, n (%)	4 (20)
Moderate intensity, n (%)	11 (55)
High intensity, n (%)	4 (20)
iRAAS, n (%)	13 (65)
β-blockers, n (%)	12 (60)
Furosemide, n (%)	12 (60)
Calcium channel blockers, n (%)	3 (15)
Nitrate, n (%)	5 (25)
Amiodarone, n (%)	1 (5)

DOAC, direct oral anticoagulants; iRAAS, inhibitors of renin-angiotensin-aldosterone system.

Table 3. Aged-matched control group characteristics.

		p
N	20	
Age, years, median (IQR)	92 (90-94)	0.862
Female, n (%)	14 (70)	0.304
Cardiovascular risk factors		
Hypertension, n (%)	17 (85)	0.733
Dyslipidemia, n (%)	8 (42)	0.657
Diabetes, n (%)	6 (30)	0.096
Smoker or previous smoker, n (%)	1 (5)	0.273
Atrial fibrillation, n (%)	3 (15)	0.328
Chronic kidney disease, n (%)	6 (30)	0.435
Modified rankin scale, median (IQR)	2 (1-3)	0.948
Acute event		
STEMI, n (%)	7 (35)	<0.001
Anterior, n (%)	3 (43)	0.215
Inferior, n (%)	2 (29)	
Posterior, n (%)	1 (14)	
Infero-lateral, n (%)	1 (14)	
Infarction of indeterminate location, n (%)	6 (30)	
NSTEACS, n (%)	7 (35)	
High-sensitivity troponin I, ng/L, median (IQR)	83,509 (7425-162,034)	0.047
Brain natriuretic peptide, pg/mL, median (IQR)	427 (223-969)	0.251
Admission hemoglobin, g/dL, median (IQR)	12.3 (12.0-12.9)	0.166
Killip class		0.388
I, n (%)	8 (40)	
II, n (%)	8 (40)	
III, n (%)	2 (10)	
IV, n (%)	2 (10)	
Left ventricle systolic function		0.952
Normal, n (%)	8 (40)	
Mildly reduced, n (%)	3 (15)	
Moderately reduced, n (%)	4 (20)	
Severely reduced, n (%)	5 (25)	
In-hospital mortality	5 (25)	0.319

IQR, interquartile range; STEMI, ST-elevation myocardial infarction; NSTEACS, non-ST elevation-acute coronary syndrome.

populations. Eighty studies enrolled older patients (> 80 years) with non-ST-ACS and showed a reduction in the ischemic composite endpoint (myocardial infarction, need for urgent revascularization, stroke, and death) in the group assigned to the invasive strategy. However, the authors found a dilution of the efficacy of the invasive strategy with increasing age and questioned its value for patients older than 90 years [9]. Recently, Wyk *et al*. published a review of trials from January 1990 to May 2022 that compared clinical outcomes in frail patients 75 years of age or older submitted to different coronary interventions; results tend to support invasive treatment, but the data was not very robust and had a high risk of bias [5].

Our study was unique in that it evaluated only nonagenarians submitted to emergency CA and provided information about the characteristics and outcomes of this very elderly population. For around a decade, we enrolled 34 patients and compared them to an age-matched population. Patients had a high burden of cardiovascular risk factors and other comorbidities such as chronic kidney disease and cerebrovascular disease. Even with the possibly obvious bias in candidates for invasive coronarography (since patients whose CA was considered futile were previously excluded), it was a population with already some degree of disability.

The main reason to proceed with emergency CA was STEMI, particularly anterior infarction, with left anterior descending artery as the culprit in most cases. As expected, since extensive coronary artery disease was described in previous reports from 80-plus populations [10,11], more than half of the patients presented multivessel disease.

Most patients evolved in at least class II or more of Killip, with an important number of patients in Killip IV; also, more than two-thirds developed left ventricle systolic dysfunction, which reveals the aggressive nature of an ACS in this super elderly population, even with guideline-oriented therapy. The mortality rate was very high during the index event, both in the study and in the control group.

Regarding medication, there was a tendency to add clopidogrel instead of a more potent P2Y12 inhibitor as the second antiaggregant, which explains the presumably higher risk of bleeding in this vulnerable population. The Popular Age trial, published in 2020, also favors clopidogrel over ticagrelor in patients older than 70 years old due to fewer bleeding events without an increase in the combined endpoint of all-cause death, myocardial infarction, stroke, and bleeding [12]. In our study, only about one-third of patients were medicated with iRAAS, or b-blockers, mainly due to hypotension. A few patients were not on BB due to an auriculoventricular conduction disturbance. In ambulatory, most patients develop symptomatic heart failure, needing loop-diuretic.

One of the main goals of our study was to compare this population submitted to the considered best care with an aged-matched control group that was not submitted to emergency CA. Neither mortality in the index event or during 5 years of follow-up nor MACE occurrence were statistically different between the two groups. It is possible that patients in the control group had a better clinical and hemodynamic status, so they did not proceed to emergency CA, and the prognosis of the study group came closer to that thanks to emergency CA. On the other hand, due to the retrospective nature of this study, we could not exclude a possible selection bias in which emergency CA was preferentially performed in STEMI patients with a better functional profile and fewer comorbidities. Hence, the high in-hospital and follow-up mortality and the high rate of adverse events in the two groups showed how super-elderly patients are a special vulnerable population. As doctors, we must provide the best treatment options without pursuing unreliable objectives or therapeutic futility.

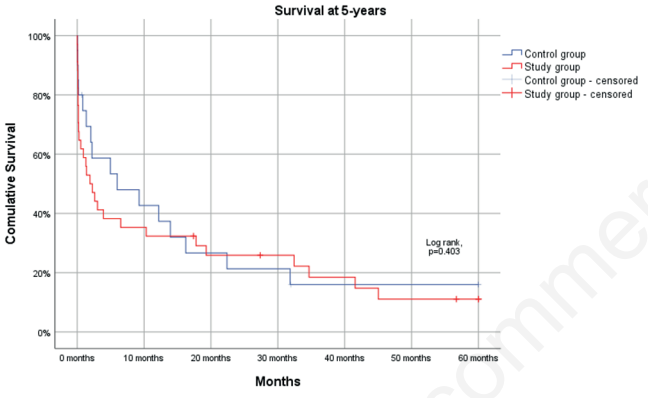

Figure 1. Survival analysis. There was no significant difference in mortality between the two groups (Log-rank, p=0.403) and more than 50% of patients died in 2 years in both groups.

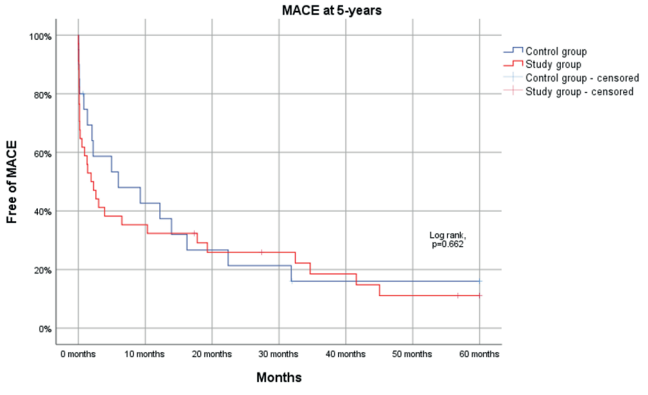

Figure 2. Time-to-adverse-event analysis. Both groups were similar concerning major adverse cardiovascular events occurrence, with more than 80% having at least one event in 5 years. MACE, major adverse cardiovascular events.

Limitations

The primary limitation of this study was the relatively small sample size, which precludes major conclusions regarding associations and/or correlations. This is a retrospective and observational analysis. Also, a nested case-control study could have been more appropriate than the age-matched control population used in our study. Our results should be interpreted with caution, and larger prospective trials should be done to confirm them.

Conclusions

Our cohort of super-elderly patients submitted to emergency CA showed a high rate of multivessel disease, and most patients evolved into at least class II of Killip with left ventricular dysfunction. In-hospital mortality was high and similar to that of an aged-matched control group not submitted to an emergency CA. Also, during a 5-year follow-up, they showed no survival or MACE benefit compared to the control group. Despite being a small study, these findings highlight the efforts that should be made to optimize care in this vulnerable population, underrepresented in clinical trials; risks and benefits should be taken into account to avoid possible unnecessary discomfort in this setting.

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