IJC Heart & Vasculature 40 (2022) 101036

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: www.sciencedirect.com/journal/ijc-heart-and-vasculature

"Impact of age on management and prognosis of resuscitated sudden cardiac death patients"

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ARTICLE INFO

Keywords:
Sudden cardiac death
Elderly patients
Neurological outcomes

ABSTRACT

Background: Sudden cardiac death (SCD) has a great impact on healthcare due to cardiologic and neurological complications. Admissions of elderly people in Cardiology Intensive Care Units have increased. We assessed the impact of age in presentation, therapeutic management and in vital and neurological prognosis of SCD patients.
Methods: We carried out a retrospective, observational, multicenter registry of patients who were admitted with a SCD in 5 tertiary hospitals from January 2013 to December 2020. We divided our cohort into two groups (patients < 80 years and ≥ 80 years). Clinical, analytical and hemodynamic variables as well as in-hospital management were registered and compared between groups. The degree of neurological dysfunction, vital status at discharge and the influence of age on them were also reviewed.
Results: We reviewed 1160 patients admitted with a SCD. 11.3% were ≥ 80 years. Use of new antiplatelet agents, performance of a coronary angiography, use of pulmonary artery catheter and temperature control were less carried out in the elderly. Age, non-shockable rhythm, Killip class > 1 at admission, time to CPR initiation > 5 min, time to ROSC > 20 min and lactate > 2 mmol/L were independent predictors for in-hospital mortality. Non-shockable rhythm, Killip class > 1 at admission, time to CPR initiation > 5 min and time to ROSC > 20 min but not age were independent predictors for poor neurological outcomes.
Conclusions: Age determined a less aggressive management and it was associated with a worse vital prognosis in patients admitted with a SCD. Nevertheless, age was not associated with worse neurological outcomes.

1. Introduction

Sudden cardiac death (SCD) is defined as an unexpected cardiac arrest due to a heart condition, that occurs within one hour of symptoms onset. Nowadays, it represents the third leading cause of death in Europe (15–20%) and accounts for 50% of cardiovascular deaths in Western

Abbreviations: SCD, Sudden cardiac death; CPR, Cardiopulmonary resuscitation; ROSC, Recovery of spontaneous circulation; CA, Cardiac arrest; ADL, Activities of daily living; EI-MV, Endotracheal intubation with mechanical ventilation; CAG, Coronary angiography; TC, Temperature control; NSE, Neuronal specific enolase; CPC, Cerebral performance category; CCI, Charlson Comorbidity Index.

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https://doi.org/10.1016/j.ijcha.2022.101036
Received 20 January 2022; Received in revised form 27 March 2022; Accepted 18 April 2022
Available online 27 April 2022

societies [1,2].

Pre-hospital care protocols for SCD patients and the spread of cardiopulmonary resuscitation (CPR) / automated external defibrillator (AED) training courses together with the progressive aging of the population have increased the number of elderly patients admitted to Cardiology Intensive Care Units (CICU) with an aborted SCD [3–5]. Impact of SCD patients on health care systems is high due to cardiologic and mainly neurologic complications that could lead to poor vital and functional prognosis of these patients [6]. This is especially relevant in the elderly since morbidity and disability clearly increase with age, further worsening their vital and neurologic prognosis.

Even though the development of standardized protocols have improved the prognosis of patients hospitalized after SCD [7,8], their mortality and morbidity, especially in the older population, remain unacceptably high. Moreover, elderly patients are usually underrepresented in clinical trials, so the evidence for some techniques or procedures in this setting is limited. For instance, they may not receive some of the medical therapies that have been reported to improve the prognosis based on the assumption of a per se poor prognosis [9,10]. Although cardiac arrest guidelines, ethical statements, and clinical procedures do not propose age as a criterion for discrimination in SCD care [11], physicians are often faced with having to decide whether certain diagnostic tests or therapies may be beneficial or futile in older patients [12].

The aim of this observational study is to assess whether the age could have an influence in the etiology, clinical presentation and therapeutical management of patients admitted with a SCD in tertiary hospitals. Furthermore, we aimed to evaluate whether these possible differences could affect vital and neurological outcomes of these patients.

2. Methods

2.1. Study population

In this retrospective study, we reviewed all consecutive patients admitted from January 2013 to December 2020 with an aborted SCD to CICUs of 5 third-level hospitals in Catalonia, Spain (Hospital Universitario Dr. Josep Trueta, Hospital Universitario de Bellvitge, Hospital Universitario Joan XXIII, Hospital Universitario Germans Trias i Pujol and Hospital de la Santa Creu i Sant Pau). Inclusion criteria were: a) $\geq$ 18 years of age and b) diagnosis of SCD according to current guidelines [1,2]. Exclusion criteria were: a) patients not recovered from SCD prior to hospital admission and b) cardiac arrest (CA) due to an extracardiac condition.

The study was conducted in accordance with the standards set by the "Declaration of Helsinki" and was approved by the Clinical Research Ethics Committe. Informed consent was waived due to the retrospective nature of the study.

2.2. Study variables

Patient-related factors were collected from medical reports or by anamnesis to relatives at admission. We divided our cohort in two groups as follows: the "younger" group refers to patients $<$ 80 years while the "older" or "elderly" group refers to patients $\geq$ 80 years. This cut-off age was chosen to achieve a better differentiation between the two groups. We identified those patients who were dependent for the basic activities of daily living (ADL) and we calculated the Charlson Comorbidity Index (CCI) [13]. Biochemical and hematological parameters were measured by standard procedures in first blood test and arterial blood gas samples at admission; the estimated glomerular function rate was calculated by the Modification of Diet in Renal Disease Study equation (MDRD) [14].

We considered resuscitation parameters such as location of CA, witnessed CA, initial recorded rhythm, use of AED and resuscitation times. Time to CPR initiation was defined as the time from cardiac arrest to the initiation of CPR maneuvers (by health or non-health personnel). Shockable rhythm was considered if ventricular fibrillation (VF), pulseless ventricular tachycardia (VT), or shockable rhythm according to AED were the first rhythms obtained. All these resuscitation parameters were collected from medical emergency services reports. First EKG post ROSC achieved and hemodynamic variables upon arrival at the hospital were also analyzed.

Management during hospital admission was at the discretion of the treating physician and according to availability in each hospital. Percentage of endotracheal intubation with mechanical ventilation (EI-MV), use of inotropes, intra-aortic balloon pump (IABP), pulmonary artery catheter (PAC), renal replacement therapy (RRT) as well as coronary angiography (CAG) performance and emergency/urgent percutaneous coronary intervention (PCI) were reported. In patients who underwent CAG, number of affected vessels, culprit vessel and TIMI flow grade after PCI were also recorded.

Temperature control (TC) was performed using surface or endovascular cooling devices according to availability in each hospital at a temperature of 33 °C. TC complications and reasons not to start or to stop it were examined. We also reviewed the presence of myoclonus or status epilepticus as well as the performance of an electroencephalogram (EEG), use of anticonvulsant medication or the induction of a barbiturate coma. We registered the absence of brain stem reflexes and spontaneous mobilization at 72 h after SCD. Performance of somatosensory evoked potentials N20 (SSEP-N20) and brain magnetic resonance imaging (MRI) were also recorded. We registered neuronal specific enolase (NSE) at 24 h, 48 h and 72 h if available. To categorize neurological function at discharge, the Cerebral Performance Category (CPC) scale was used [15]. For patients who died from non-neurological causes, the last known previously achieved CPC category was considered. If the patient died from a non-neurological cause before a CPC category could be established (i.e., patients who died while still under sedation with no possibility of CPC assessment) it was categorized as unknown CPC. The population was divided into 2 groups: good neurological prognosis (CPC 1-CPC 2) and poor neurological prognosis (CPC 3-CPC 5). Patients with unknown CPC were excluded from neurological prognosis analysis. Restriction of invasive procedures as well as in-hospital mortality and causes of death were also registered.

2.3. Statistical analysis

Results are presented as the mean (standard deviation) for continuous variables with a normal distribution, medians for continuous variables with a non-Gaussian distribution, and percentages for categorical variables. The characteristics of patients with age $<$ 80 years and age $\geq$ 80 years were compared using the x^2 test or Fisher exact test for categorical variables. For quantitative variables, they were analyzed by *t*-test in the case of normal distribution, or Mann-Whitney *U* test in the case of a non-normal distribution.

Multivariate analysis to evaluate the effect of variables on the incidence of in-hospital mortality and neurologic prognosis at discharge were performed using Cox proportional hazard modelling that included terms that showed $p < 0.1$ in the univariate analysis, as well as those previously reported to provide prognostic information [16]. Significance level was set at $p < 0.05$. All statistical analyses were performed using Stata 13.0 for Windows.

3. Results

The 5 participating centers recorded 1160 patients with an aborted SCD between 2013 and 2020. One hundred and thirty-one patients (11.3%) were $\geq$ 80 years and 27 patients (2.3%) were dependent for the basic ADL.

3.1. Differences in baseline characteristics between groups

Differences in baseline characteristics at admission of both groups are detailed in Table 1. Patients aged ≥ 80 years were more frequently women, hypertensive, diabetic and dyslipidemic. In addition, there was also a higher percentage of patients with a history of coronary artery disease, respiratory disease, cerebrovascular disease and chronic kidney disease in older patients. As expected, patients ≥ 80 years had a higher CCI and they were in more percentage dependents for basic ADL.

Regarding the location of the CA, in elderly patients, it occurred more frequently in a healthcare center and less frequently in a public place or at home. They had a lower percentage of a first shockable rhythm and a shorter time to ROSC, but no differences were found in percentage of witnessed SCD or in time to initiation of CPR.

When ROSC was achieved, elderly patients more frequently presented a first EKG without repolarization alterations or with left bundle branch block, while in younger patients a higher proportion of ST segment elevation was documented. Recovery of sinus rhythm was also lower in the older group.

No differences were found in systolic blood pressure or LVEF upon hospital arrival. First arterial blood gases showed a better pH value in elderly patients, while no differences were recorded in lactate levels. First blood test showed that older group had a lower glomerular filtration and a lower hemoglobin and white blood cells count. No other analytical or hemodynamic differences were found between groups.

3.2. Differences in etiology and therapeutic management between groups

Differences in etiology of SCD and therapeutic management of both groups are detailed in Table 2. In the elderly group, the percentage of SCD attributed to STEMI was lower while that attributed to bradyarrhythmias and dilated ischemic cardiomyopathy was higher than in younger patients.

No differences were found in the percentage of either anterior STEMI location or in Killip class > 1. Use of inotropes and IABP did not differ between groups, but PAC was less used in elderly patients even after excluding those patients dependent for basic ADL. ECMO was started in only 1.9% of the cases (21 patients), all of them < 80 years old.

An emergent CAG was performed less frequently in older patients. Although there was a lower percentage of patients with ST segment elevation in the elderly group, if we only included patients with elevated ST on the baseline EKG, differences were still significant. Differences were maintained despite excluding from the analysis patients who were dependent for basic ADL. No differences were found in the percentage of PCI performed or in the initial TIMI grade flow, but a significant lower use of new antiplatelet agents and a higher proportion of TIMI grade flow < 3 after PCI were shown in older patients.

The use of TC showed significant differences between groups. TC was induced in a smaller percentage of the elderly patients and significance was maintained despite including only patients who had pulseless VT/VF as the first rhythm. After excluding patients who were dependent for basic ADL, the differences remained significant. No differences were documented in the percentage of early withdrawal from TC in both groups.

3.3. Differences in prognostic stratification and outcomes between groups

Clinical previously established indicators of poor outcome (status myoclonus ≤ 72 h, absence of stem reflexes at ≥ 72 h and absence of spontaneous movements other than extension ≥ 72 h) did not differ between groups. Similarly, no differences were found in status epilepticus, use of anticonvulsant medication or induction of barbiturate coma percentage. A lower percentage of EEGs was performed in the group of elderly people. Moreover, a lower number of SSEP-N20 and brain MRI tests were also requested in older patients even though no differences in percentage of cerebral tomography were found between

Table 1
Differences between baseline characteristics at admission.

Characteristic	All cohort (n = 1160)	Patients < 80 years (n = 1029)	Patients ≥ 80 years (n = 131)	P-value
BASELINE				
Age (years)	64.1 (53.9–73.6)	61.7 (52.5–70.1)	83.0 (81.6–85.5)	<0.001
Male gender, %	74.2 (861/1160)	75.7 (779/1029)	62.6 (82/131)	0.001
Dependent for basic ADL, %	2.3 (27/1160)	1.4 (14/1029)	10.0 (13/131)	<0.001
Charlston comorbidity index	3 (1–4)	2 (1–4)	5 (4–6)	<0.001
Hypertension, %	57.9 (672/1160)	54.8 (564/1029)	82.4 (108/131)	<0.001
Diabetes mellitus, %	26.7 (309/1160)	25.7 (264/1029)	34.4 (45/131)	0.035
Dyslipidemia, %	49.5 (574/1160)	48.3 (497/1029)	58.8 (77/131)	0.024
Current smoker, %	35.8 (415/1159)	38.2 (393/1029)	16.9 (22/130)	<0.001
Body mass index (kg/m^2)	25.4 (24.2–29.4)	25.4 (24.2–29.4)	25.0 (24.2–27.8)	0.194
Previous coronary artery disease, %	22.8 (264/1160)	21.8 (224/1029)	30.5 (40/131)	0.024
Respiratory disease, %	13.1 (152/1160)	12.3 (127/1029)	19.1 (25/131)	0.031
Chronic kidney disease, %	10.6 (123/1160)	8.6 (88/1029)	26.7 (35/131)	<0.001
Cerebrovascular disease, %	7.8 (91/1160)	7.0 (72/1029)	14.5 (19/131)	0.003
CARDIAC ARREST PARAMETERS				
Location of CA:, %				<0.001
- Healthcare centre	22.0 (255/1160)	20.1 (207/1029)	36.6 (48/131)	
- Home	34.3 (398/1160)	35.1 (361/1029)	28.2 (37/131)	
- Public place	43.7 (507/1160)	44.8 (461/1029)	35.1 (46/131)	
Witnessed CA, %	91.3 (1059/1160)	91.5 (941/1029)	90.1 (118/131)	0.600
First shockable rhythm, %	70.4 (814/1157)	72.4 (743/1026)	54.2 (71/131)	<0.001
AEDs use, %	32.2 (364/1130)	32.4 (330/1020)	30.9 (34/110)	0.453
Time until initiation of CPR (min)	2 (0–5)	2 (0–5)	1 (0–3.5)	0.109
Time until ROSC (min)	22 (13–33)	23 (13–35)	20 (9–30)	0.0016
BASELINE EKG & ECHO VARIABLES				
Sinus rhythm, %	71.0 (804/1132)	73.8 (745/1010)	48.4 (59/122)	<0.001
First EKG abnormalities:, %				
- No abnormalities	12.1 (137/1134)	11.2 (113/1010)	19.7 (24/122)	0.009
- ST segment elevation	46.8 (531/1134)	49.0 (495/1010)	29.5 (36/122)	<0.001
- ST segment depression	15.7 (178/1134)	15.2 (154/1010)	19.7 (24/122)	0.25
- Negative T waves	4.1 (47/1134)	4.3 (43/1010)	3.3 (4/122)	0.577
- Left bundle branch block	11.6 (131/1134)	10.6 (107/1010)	19.7 (24/122)	0.004
- Right bundle branch block	7.9 (90/1134)	7.9 (80/1010)	8.2 (10/122)	0.973
LVEF:, %				0.981
- Preserved	29.0 (313/1079)	29.0 (279/961)	28.8 (34/118)	
- Mildly depressed	16.1 (174/1079)	16.0 (154/961)	17.0 (20/118)	
- Moderately depressed	41.1 (443/1079)	41.0 (394/961)	41.5 (49/118)	

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Table 1 (*continued*)

Characteristic	All cohort (n = 1160)	Patients < 80 years (n = 1029)	Patients ≥ 80 years (n = 131)	P-value
- Severely depressed	13.8 (149/1079)	13.9 (134/961)	12.7 (15/118)	
ANALYTICAL & HEMODYNAMIC VARIABLES				
Systolic blood pressure (mmHg)	106 (87–127)	107 (87–127)	105 (85–126)	0.950
Heart rate (bpm)	84 (68–95)	85 (64–96)	79 (62–85)	0.356
pH	7.23 (7.10–7.31)	7.22 (7.10–7.31)	7.27 (7.09–7.36)	0.008
Lactate (mmol/L)	5.2 (2.7–8.7)	5.2 (2.6–8.8)	5.2 (2.9–8.2)	0.618
eGFR (ml/min/1.73 m^2)	60.0 (44.1–78.4)	61.5 (46.0–79.1)	44.7 (31.5–65.6)	<0.001
AST (U/L)	106.5 (53–209)	107 (54–206)	96 (41–248)	0.988
Hemoglobin (g/L)	135 (117–149)	136 (119.5–151)	121 (106–137)	<0.001
Leukocytes (x10^9/L)	14.4 (10.9–18.9)	14.6 (11.0–19.1)	12.5 (9.2–15.7)	0.002
Platelets (x10^3/mm^3)	208 (169–261)	211 (171–262)	198 (148–247)	0.085
C-reactive protein (mg/dl)	9.5 (2.5–62.2)	8.5 (2.4–57.7)	13.0 (4.1–69.7)	0.215

Continuous variables are expressed as median (IQR) and categorical data as % (n).
ADL: Activities of daily living; CPR: Cardiopulmonary resuscitation; CA: cardiac arrest; AED: Automatic external defibrillator; EKG: Electrocardiogram; ROSC: Recovery-of-spontaneous-circulation; LVEF: Left ventricle ejection fraction; eGFR: Estimated glomerular filtration rate; IQR: interquartile range.

groups. In addition, a NSE determination was carried out less frequently in patients ≥ 80 years. There were no differences in the percentage of neither pathological values of NSE (>33 ng/L) nor in positive Δ-NSE between groups if repeated NSE determinations were performed.

In-hospital mortality was significantly higher in the elderly group. Anoxic encephalopathy was more common in younger patients whilst cardiovascular death was more frequently the cause of death in older patients. Restriction of invasive procedures was more commonly performed in the patients ≥ 80 years.

There were no differences in the percentage of patients with a good neurological prognosis between both groups. The percentage of patients with unknown CPC was higher in the elderly. Differences in prognostic stratification and outcomes between groups are presented Table 3.

3.4. Predictors of in-hospital mortality

A univariate analysis was performed to assess variables associated with in-hospital mortality. A Cox proportional hazard regression analysis was performed including the well-known outcome predictors in SCD patients and those variables found statistically significant in the univariate analysis. Age, non-shockable rhythm, time to to CPR initiation > 5 min, time to ROSC > 20 min, a Killip class > 1 and lactate > 2 mmol/L at admission were independent predictors associated with in-hospital mortality in these patients. Detailed results are shown in Table 4.

3.5. Predictors of poor neurologic outcome

We performed a univariate analysis to identify prognostic variables of poor neurologic outcomes among pacients in whom CPC assessment was available. Based on the variables with p value < 0.1 in the univariate analysis those with a known prognostic value in the neurological outcomes of patients with SCD, a Cox proportional hazard regression analysis was performed. A non-shockable rhythm, time to CPR initiation > 5 min, time to ROSC > 20 min and Killip class > 1 at admission were

Table 2
Differences in etiology and therapeutic management.

Characteristic	All cohort (n = 1160)	Patients < 80 years (n = 1029)	Patients ≥ 80 years (n = 131)	P-value
ETIOLOGY				
Ischuemic etiology, %	68.2 (786/1152)	69.1 (706/1022)	61.5 (80/130)	0.085
STEMI, %	43.4 (501/1154)	45.2 (463/1024)	29.2 (38/130)	0.001
- Anterior STEMI location	50.9 (255/501)	50.5 (234/463)	55.3 (21/38)	0.576
NSTEMI, %	10.4 (120/1154)	10.1 (103/1024)	13.1 (17/130)	0.286
Dilated ischemic cardiomyopathy, %	14.2 (164/1154)	13.5 (138/1024)	20.0 (26/130)	0.034
Bradyarrhythmia, %	3.2 (37/1156)	1.8 (18/1026)	14.6 (19/130)	<0.001
Dilated non-ischemic cardiomyopathy, %	7.0 (81/1157)	7.3 (75/1027)	4.6 (6/130)	0.256
Hypertrophic cardiomyopathy, %	1.1 (13/1156)	1.3 (13/1026)	0.0 (0/130)	0.197
Valvular heart disease, %	2.4 (28/1156)	2.2 (23/1028)	3.9 (5/128)	0.263
Idiopathic, %	12.6 (145/1151)	12.7 (130/1021)	11.5 (15/130)	0.711
THERAPEUTIC MANAGEMENT				
Inotropes, %	44.6 (507/1137)	44.2 (448/1014)	47.9 (59/123)	0.430
Intra-aortic counterpulsation balloon, %	8.5 (96/1129)	8.9 (90/1007)	4.9 (6/122)	0.130
Pulmonary artery catheter, %	11.6 (96/828)	12.8 (94/733)	2.1 (2/95)	0.002
- Excluding depenent for basic ADL	11.9 (96/807)	12.9 (94/727)	2.5 (2/80)	0.006
Renal replacement theraphy, %	6.7 (56/836)	7.3 (54/741)	2.1 (2/95)	0.056
Emergent CAG, %	69.6 (799/1148)	72.8 (742/1019)	44.2 (57/129)	<0.001
- CAG if ST elevation	91.7 (486/530)	92.5 (457/494)	80.6 (29/36)	0.012
- CAG if ST elevation and excluding depenent for basic ADL	91.6 (481/525)	92.5 (455/492)	78.8 (26/33)	0.006
Emergent PCI if CAG, %	55.5 (437/787)	55.1 (403/731)	60.7 (34/56)	0.411
Deferred CAG, %	8.1 (92/1136)	8.2 (83/1009)	7.1 (9/127)	0.668
Use of new antiplatelet agents, %	46.7 (541/1158)	49.1 (506/1030)	27.4 (35/128)	<0.001
Culprit artery:, %				
- Left main	5.8 (30/517)	6.1 (29/479)	2.6 (1/38)	0.370
- Left anterior descending	42.5 (220/518)	45.1 (208/461)	21.1 (12/36)	0.075
- Left circumflex artery	19.7 (102/518)	18.4 (88/478)	35.0 (14/40)	0.008
- Right coronary artery	29.2 (151/517)	29.3 (140/478)	28.2 (11/39)	0.893
- Multivessel disease				0.002

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Table 2 (*continued*)

Characteristic	All cohort (n = 1160)	Patients < 80 years (n = 1029)	Patients ≥ 80 years (n = 131)	P-value
	35.6 (313/879)	34.2 (279/816)	54.0 (34/63)	
Initial TIMI grade flow < 3, %	49.6 (413/832)	49.6 (385/776)	50 (28/56)	0.940
Final TIMI grade flow < 3, %	10.4 (87/837)	9.8 (76/781)	19.6 (11/56)	0.020
TC, %	53.4 (616/1154)	56.5 (580/1026)	28.1 (36/128)	<0.001
TC if first shockable rhythm, %	59.3 (481/811)	61.3 (455/742)	37.7 (26/69)	<0.001
TC if first shockable rhythm excluding depenent for basic ADL, %	59.6 (477/800)	61.6 (453/736)	37.5 (24/64)	<0.001
TC early withdrawal, %	12.3 (75/610)	12.6 (72/571)	8.3 (3/36)	0.454

All variables are expressed as % (n).
STEMI: ST-elevation myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; ADL: Activities daily living; CAG: coronary angiography; OHCA: out-of-hospital cardiac arrest; PCI: percutaneous intervention; TC: temperature management.

independent predictors of poor neurological outcome. Age was not a predictor of poor neurological prognosis in these patients. Detailed results are listed in Table 5.

General management and predictors of in-hospital mortality and poor neurologic outcomes are illustrated in Fig. 1.

4. Discussion

To the best of our knowledge this is the largest cohort addressing the impact of age on the management and prognosis of patients with an aborted SCD. Our study has shown the following main findings: 1) age was an independent predictor for in-hospital mortality in patients admitted to hospital after an aborted SCD, 2) elderly patients were less frequently offered therapies that are currently part of the standard of care in SCD patients and 3) neurological prognosis of elderly patients that suffered an aborted SCD appeared to be similar to that of younger patients.

First, advanced age seems to be an independent predictor of in-hospital mortality in patients admitted with a SCD. Our results are aligned with previous studies confirming a higher in-hospital mortality in SCD patients. As described in previous studies [17–20], we found that younger patients had a higher likelihood of survival compared with elderly patients admitted after a SCD. Interestingly, the impact of age for increased mortality was lower with respect to other variables associated with poorer prognosis such as an initial non-shockable rhythm or long resuscitation times. This is supported by the results of previous studies such as Hirlekar et al [21] who reported that despite the fact that the 30-day survival of patients with SCD decreases with age, its OR was low, suggesting that age would be a weak predictor for the vital prognosis of these patients. For this reason, we looked for possible additional causes that could explain this large difference in mortality between groups such as a distinct diagnostic and therapeutic approach.

The management of elderly patients admitted to hospital with a SCD was different from that of younger patients. Although the role of CAG after a SCD is still debated, the guidelines propose that an emergent CAG should be indicated in those patients with the highest risk of a coronary occlusion (ST-segment elevation on the initial EKG, hemodynamic and/

Table 3
Differences in prognostic stratification and outcomes between groups.

Characteristic	All cohort (n = 1160)	Patients < 80 years (n = 1029)	Patients ≥ 80 years (n = 131)	P-value
Status myoclonus ≥ 72 h, % (1096)	19.8 (217/1096)	20.2 (198/978)	16.1 (19/118)	0.293
Absence of stem reflexes ≥ 72 h, %	17.9 (151/844)	17.7 (135/763)	19.8 (16/81)	0.867
Absence of spontaneous movements other than extension ≥ 72 h, %	30.5 (245/803)	31.2 (225/722)	24.7 (20/81)	0.233
EEG, %	39.9 (442/1108)	41.1 (406/988)	30.0 (36/120)	0.019
Status epilepticus, %	24.7 (120/486)	25.6 (112/437)	16.3 (8/49)	0.152
Use of anticonvulsant medication, %	17.9 (197/1100)	18.5 (181/982)	13.6 (16/118)	0.189
Induction of barbiturate coma, %	3.5 (23/657)	3.8 (22/579)	1.3 (1/78)	0.279
NSE determination, %	54.9 (608/1107)	57.5 (567/987)	34.1 (41/120)	<0.001
NSE > 33 ng/L, %	45.0 (125/278)	44.6 (115/258)	50 (10/20)	0.638
Positive Δ-NSE, %	47.6 (88/185)	46.8 (81/173)	58.3 (7/12)	0.440
SSEP-N20, %	28.8 (318/1104)	30.1 (296/985)	18.5 (22/119)	0.009
Brain magnetic resonance imaging, %	16.2 (166/1025)	17.0 (156/918)	9.3 (10/107)	0.030
Cerebral tomography, %	45.7 (404/884)	46.2 (366/792)	41.3 (38/92)	0.377
CPC:, %				
- 1	42.8 (497/1160)	43.8 (451/1029)	35.1 (46/131)	0.058
- 2	6.1 (71/1160)	6.4 (66/1029)	3.8 (5/131)	0.243
- 3	4.6 (53/1160)	4.9 (50/1029)	2.3 (3/131)	0.185
- 4	21.4 (248/1160)	21.7 (223/1029)	19.1 (25/131)	0.496
- 5	4.6 (55/1160)	4.9 (50/1029)	3.8 (5/131)	0.597
- Unknown	20.3 (236/1160)	18.3 (189/1029)	35.9 (47/131)	<0.001
CPC 1–2, %	61.5 (568/923)	61.6 (517/839)	60.7 (51/84)	0.881
Restriction of invasive procedures, %	30.3 (226/746)	28.7 (189/658)	42.0 (37/88)	0.011
In-hospital mortality, %	44.2 (513/1160)	42.2 (434/1029)	60.3 (79/131)	<0.001
- Anoxic encephalopathy	55.4 (284/513)	57.4 (249/434)	44.3 (35/79)	0.032
- Cardiovascular death	30.2 (149/493)	27.6 (115/417)	44.7 (34/76)	0.003

All variables are expressed as % (n).
EEG: Electroencephalogram; NSE: Neuron specific enolase; SSEP-N20: Somatosensory evoked potentials N20; CPC: Cerebral Performance Category STEMI: ST-

elevation myocardial infarction; NSTEMI: non ST-elevation myocardial infarction; ADL: Activities daily living; CAG: coronary angiography; PCI: percutaneous intervention; TC: temperature management.

or electrical instability) [22] while in cases where there are no classical signs of STEMI in EKG, an immediate CAG strategy appears not to be superior to a delayed angiography strategy [23]. In our study, CAG was performed less frequently in the elderly patients. This could be explained by a lower percentage of ST-elevation in this group, but when we analyzed only patients with ST-elevation, the percentage of emergent CAG in the elderly was still lower than in the younger group. Early CAG has been associated with better outcomes regardless of age in patients who presented out-of-hospital SCD with a shockable rhythm [24] being also less frequently performed in the elderly group in our cohort.

Table 4
Predictors of in-hospital mortality. Univariate and multivariate analysis (n = 1160).

UNIVARIATE ANALYSIS				MULTIVARIABLE ANALYSIS		
Characteristic	**Alive (n = 647)**	**Dead (n = 513)**	**p-value**	**Characteristic**	**HR (95% CI)**	**p-value**
Age (years)	61.3 (51.7–72.1)	67.1 (57.7–75.5)	<0.001	Age	1.04 (1.01–1.08)	0.009
Male gender, %	74.7 (483/647)	73.7 (378/513)	0.708			
Hypertension, %	54.7 (354/647)	62.0 (318/513)	0.013	Hypertension	0.63 (0.34–1.18)	0.149
Diabetes mellitus, %	23.8 (154/647)	30.3 (155/513)	0.013	Diabetes mellitus	2.28 (0.99–5.27)	0.054
Current smoker, %	61.4 (397/647)	67.5 (346/513)	0.031	Current smoker	1.78 (0.87–3.63)	0.114
Previous coronary artery disease, %	20.6 (133/647)	25.5 (131/513)	0.045	Previous coronary artery disease	0.55 (0.18–1.68)	0.292
Chronic kidney disease, %	8.0 (52/647)	13.8 (71/513)	0.001	Chronic kidney disease	1.12 (0.22–5.73)	0.895
Respiratory disease, %	9.9 (64/647)	17.2 (88/513)	<0.001	Respiratory disease	1.84 (0.79–4.27)	0.158
Out-of-hospital SCD, %	78.1 (505/647)	78.0 (400/513)	0.974			
Not-witnessed SCD, %	5.7 (37/647)	12.5 (64/513)	<0.001	Not-witnessed SCD	1.65 (0.87–2.25)	0.163
Non-shockable rhythm, %	14.6 (94/644)	48.6 (249/512)	<0.001	Non-shockable rhythm	3.05 (1.50–6.19)	0.002
STEMI, %	41.3 (267/647)	46.1 (234/508)	0.103			
Time to CPR initiation (min)	1 (0–5)	3 (0–6)	<0.001	Time to CPR initiation > 5 min	2.21 (1.14–4.27)	0.019
Time to ROSC (min)	17 (10–26)	30 (20–40)	<0.001	Time to ROSC > 20 min	3.14 (1.30–7.60)	0.011
SBP < 90 mmHg, %	18.0 (106/589)	37.1 (163/439)	<0.001	SBP < 90 mmHg	1.47 (0.71–3.03)	0.303
Emergent CAG	72.6 (470/647)	65.7 (329/501)	0.011	Emergent CAG	0.91 (0.55–1.35)	0.313
Multivessel disease, %	32.9 (179/544)	40.0 (134/335)	0.033	Multivessel disease	0.79 (0.42–1.48)	0.452
Final TIMI flow grade < 3, %	7.6 (39/513)	15.1 (48/318)	<0.001	Final TIMI flow grade < 3	2.09 (0.90–4.82)	0.085
Killip class > 1, %	37.5 (100/267)	65.4 (153/234)	<0.001	Killip class > 1	2.27 (1.9–4.73)	0.029
LVEF < 40%, %	36.1 (225/623)	46.3 (211/456)	0.001	LVEF < 40%	1.56 (0.77–3.16)	0.212
Lactate (mmol/L)	3.5 (1.9–6.1)	7.2 (4.6–11.4)	<0.001	Lactate > 2 mmol/L	2.45 (1.02–5.92)	0.045
eGFR (ml/min/1.73 m^2)	67.2 (51.7–82.7)	52.9 (37.8–67.9)	<0.001	eGFR (ml/min/1.73 m^2)	1.41 (0.66–2.99)	0.373
Hemoglobin (g/L)	137 (122–150)	132 (114–147)	0.005	Hemoglobin < 100 g/L	0.41 (0.06–1.1)	0.212
Leukocytes (x10^9/L)	14.1 (10.5–18.0)	15.1 (11.5–19.7)	0.003	Leukocytes > 11x10^9/L)	2.86 (0.99–8.13)	0.065

Continuous variables are expressed as median (IQR) and categorical data as % (n).
SCD: Sudden cardiac death; STEMI: ST-elevation myocardial infarction; CPR: Cardiopulmonary resuscitation; ROSC: Recovery of spontaneous circulation; CAG: Coronary angiography; LVEF: Left ventricle ejection fraction; eGFR: Estimated glomerular filtration rate; IQR: interquartile range.

Table 5
Predictors of poor neurological prognosis. Univariate and multivariate analysis (n = 1160).

UNIVARIATE ANALYSIS				MULTIVARIABLE ANALYSIS		
Characteristic	**CPC 1–2 (n = 568)**	**CPC 3–5 (n = 356)**	**p-value**	**Characteristic**	**HR (95% CI)**	**p-value**
Age (years)	61.4 (51.7–72.3)	65.1 (54.8–73.4)	0.008	Age	1.01 (0.98–1.04)	0.383
Male gender, %	74.5 (423/568)	80.1 (285/356)	0.051	Male gender	0.99 (0.41–2.35)	0.974
Hypertension, %	55.5 (315/568)	59.3 (211/356)	0.255			
Diabetes mellitus, %	24.5 (139/568)	27.8 (99/356)	0.259			
Current smoker, %	36.3 (206/568)	38.3 (136/355)	0.165			
Previous coronary artery disease, %	21.7 (123/568)	22.8 (81/356)	0.695			
Chronic kidney disease, %	8.3 (47/568)	9.8 (35/356)	0.177			
Respiratory disease, %	10.0 (57/568)	16.0 (57/356)	0.007	Respiratory disease	1.52 (0.54–4.26)	0.429
Out-of-hospital SCD, %	76.2 (433/568)	87.9 (313/356)	<0.001	Out-of-hospital SCD	1.16 (0.40–3.42)	0.781
Not-witnessed SCD, %	4.9 (28/568)	11.0 (39/356)	0.001	Not-witnessed SCD	1.37 (0.38–4.87)	0.628
Non-shockable rhythm, %	12.4 (70/566)	43.9 (156/355)	<0.001	Non-shockable rhythm	3.51 (1.85–6.64)	<0.001
Time to CPR initiation (min)	1 (0–5)	3 (1–7)	<0.001	Time to CPR initiation > 5 min	2.79 (1.44–5.41)	0.002
Time to ROSC (min)	15 (8–25)	29 (20–38)	<0.001	Time to ROSC > 20 min	3.06 (1.31–7.12)	0.009
Ischemic etiology, %	68.1 (387/568)	65.6 (233/355)	0.431			
Lactate (mmol/L)	3.3 (1.8–5.8)	6.8 (4.3–9.9)	<0.001	Lactate > 4 mmol/L	1.42 (0.67–3.01)	0.361
eGFR (ml/min/1.73 m^2)	68.7 (52.7–85.4)	54.8 (42.3–68.0)	<0.001	eGFR (ml/min/1.73 m^2)	1.49 (0.75–2.96)	0.255
Killip class > 1, %	38.2 (86/225)	49.0 (73/149)	0.039	Killip class > 1	2.26 (1.09–4.70)	0.029
Glucose (mmol/L)	11.3 (7.9–15.6)	14.9 (11.1–19.7)	<0.001	Glucose > 10 mmol/L	1.40 (0.59–3.29)	0.443
Hemoglobin (g/L)	137 (122–150)	135 (117–149)	0.266			
Leukocytes (x10^9/L)	14.0 (10.4–17.6)	15.0 (11.6–19.7)	0.003	Leukocytes > 11x10^9/L	1.83 (0.68–4.93)	0.231
SBP < 90 mmHg, %	18.2 (94/517)	25.2 (82/325)	0.015	SBP < 90 mmHg	1.16 (0.56–2.40)	0.691
LVEF < 40%, %	35.9 (195/543)	40.9 (140/342)	0.128	LVEF < 40%	0.93 (0.47–1.82)	0.826
Emergent CAG, %	71.7 (407/568)	68.5 (244/356)	0.312			
Final TIMI grade flow < 3, %	6.4 (29/453)	10.4 (25/240)	0.065	Final TIMI flow grade < 3	0.78 (0.21–2.86)	0.707
Multivessel disease, %	32.7 (156/477)	35.9 (90/251)	0.393			
No TC, %	53.1 (301/567)	68.3 (243/356)	<0.001	No TC	1.30 (0.67–2.95)	0.361

Continuous variables are expressed as median (IQR) and categorical data as % (n).
SCD: Sudden cardiac death; CPR: Cardiopulmonary resuscitation; ROSC: Recovery of spontaneous circulation; eGFR: Estimated glomerular filtration rate; SBP: systolic blood pressure; LVEF: Left ventricle ejection fraction; CAG: Coronary angiography; TC: Temperature control; IQR: interquartile range.

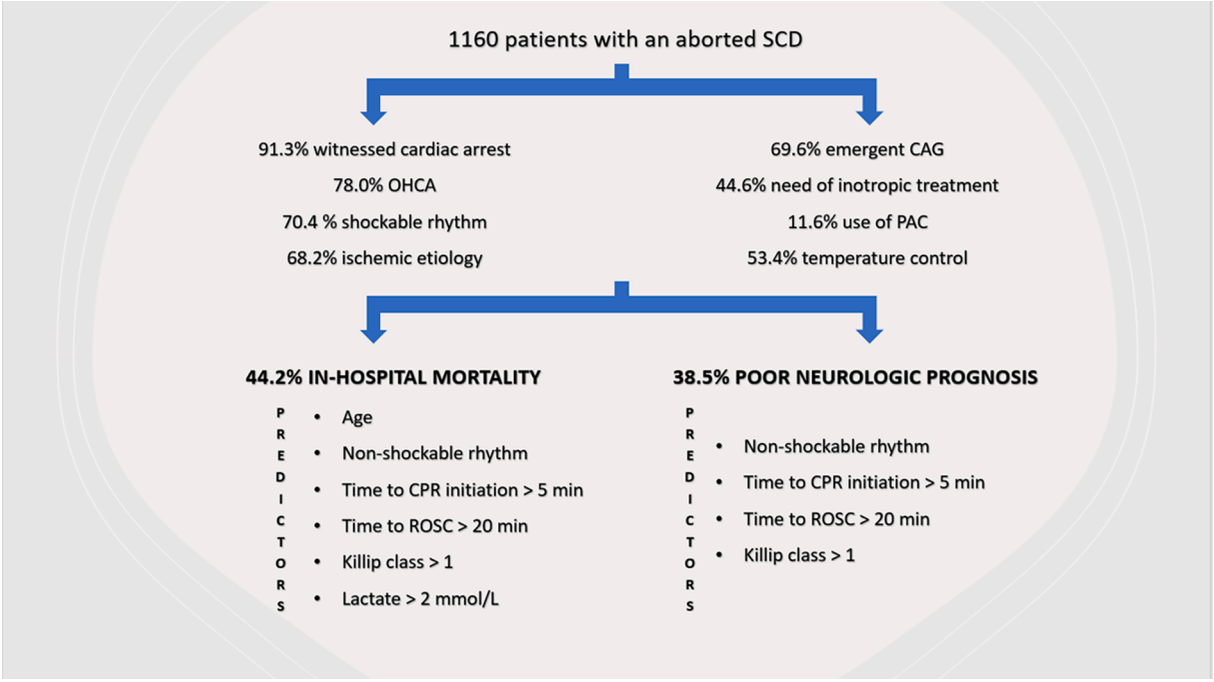

Fig. 1. General management and predictors of in-hospital mortality and poor neurologic outcomes. SCD: sudden cardiac death; CAG: coronary angiography; OHCA: out-of-hospital cardiac arrest; PAC: Pulmonary artery catheter: CPR: Cardiopulmonary resuscitation; ROSC: Recovery of spontaneous circulation.

However, our study probably lacked the power to demonstrate that it was an independent predictor for good vital prognosis.

Interestingly, among patients undergoing CAG, the rate of PCI was similar between groups, but even though they presented similar hemodynamic profile at admission, the percentage of final TIMI flow grade < 3 was higher in elderly patients. TIMI flow grade < 3 after PCI has been related to poor outcomes in patients with acute coronary syndromes [25]. In addition, as described in previous reports [26] age-related comorbidity and a higher bleeding risk could conditioned a lower use of new antiplatelet agents in the elderly group. This fact along with that age by itself can lead to an impaired coronary microcirculation state [27], could explain this higher rate of TIMI flow grade < 3 after PCI, and in turn, could also influence the outcomes.

We also observed that the use of PAC in our cohort was also lower in elderly patients. Although Sionis et al [28], found that the use of PAC was not associated with mortality in patients with cardiogenic shock, patients admitted with SCD may present hemodynamic instability not only secondary to myocardial dysfunction but also due to the effects of post-CA syndrome (ischemia–reperfusion damage) and the deleterious effects of TC (arrhythmic alterations, volume depletion due to polyuria). A better knowledge of the hemodynamic status of these patients may lead to a more adjusted and targeted management of their hemodynamics and may also influence their prognosis [29].

Although our results did not allow us to establish a causal relationship between the lower rate of CAG, the worse results of PCI and the worse hemodynamic monitoring with the higher cardiovascular mortality in the elderly group, given that there is evidence that these variables are associated with the outcomes of patients with SCD, we believe that they may have, at least partially, influenced it. Second, the influence of age on the neurological outcomes of SCD patients is still unclear. Some studies have shown that elderly patients with a SCD who survive to discharge frequently have favorable neurological outcomes similar to that of the general population [19,21,30,31]. In our setting, a prospective multicenter registry of patients with out-of-hospital SCD patients was carried out where age was not a predictor for neurological prognosis [32]. In contrast, several other studies reported age as an independent predictor of poor neurological prognosis for SCD patients [17,33,34]. In our study, after excluding patients with an unknown CPC, neurological prognosis appeared to be similar between groups, and age was not an independent predictor for neurological outcomes. Only a non-shockable rhythm, a worse hemodynamic status and longer CPR times were associated with poor neurological prognosis in our cohort.

TC is considered an effective therapy to improve neurological outcomes in patients with a SCD [35]. A recent update in the current guidelines on temperature control after cardiac arrest in adults [36] recommend actively preventing fever instead of temperature control at 32–36 °C in these patients. In our study, we found that in the elderly patients TC at 33 °C was less performed than in the younger group. Older patients presented a lower percentage of shockable rhythms which could explain the lower use of TC in this group. However, when we analyzed the use of TC only in patients with a shockable rhythm, its use in the elderly was almost half that of younger patients. Even though in the multivariate analysis, TC was not an independent predictor for neurological prognosis, it would have been interesting to know the neurological outcome of patients who died before CPC could be assessed since results could have been different [37].

Finally, the less invasive management in elderly patients admitted for SCD in our cohort could also influence their neurological prognosis, since there are studies that show an increase in survival with a favorable neurological outcome in elderly patients admitted with SCD due to a higher proportion of aggressive treatment [38].

As a piece of real-world sample, our cohort represents the whole spectrum of SCD patients admitted at CICU. Despite the improvements in management and treatment of SCD patients, we found a high morbidity and mortality in these patients. Current therapies such as extracorporeal cardiopulmonary resuscitation (ECPR) represent a promising option to improve their prognosis in certain settings [39]. However, in our environment, ECPR is not yet fully implemented. In our cohort, age was associated with the vital prognosis of patients admitted after an aborted SCD, being also a determining factor in the management and treatment of these patients. Elderly patients received less invasive treatment even though they did not present a worse clinical profile upon arrival at the hospital, which could determine, at least in part, their worse prognosis.

5. Study limitations

This is a multicenter retrospective observational study with a large cohort of patients after aborted SCD. Our study carries several limitations inherent to observational studies. The main being the impossibility of establishing causality between the differences found in elderly patients with SCD and their worse prognosis. Second, we decided to set a high age cut-off point to clearly differentiate older patients, which caused a large difference in the number of patients in each group (1029 patients $<$ 80 years vs 131 patients $>$ 80 years. In addition, given that emergency medical services can limit the therapeutic effort, there could have been a selection bias among patients who were admitted to the hospital after a SCD (decision not to EI-VM or an earlier decision to end CPR in older patients if an effective rhythm is not achieved), thus selecting those patients with higher likelihood to have a good neurological outcome. Finally, the higher non-anoxic early mortality rate in the elderly conditioned a higher percentage of patients who died before CPC could be assessed which may also have influenced the evaluation of neurological outcomes between the groups.

6. Conclusions

In conclusion, the present study shows that age plays an important role in the management and prognosis of patients admitted at CICU with an aborted SCD. A less invasive treatment of the elderly in this context could lead to an excess of mortality in these patients which would condition their worse outcomes. As the neurological prognosis of elderly patients who survive hospital admission seems to be comparable to that of younger patients, age itself should not be a reason to change the guidelines-based management of these patients. Further studies are needed to elucidate how a more invasive management of elderly patients admitted with an aborted SCD could improve their vital and neurological prognosis.

CRediT authorship contribution statement

Jordi Sans-Roselló: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Maria Vidal-Burdeus:** Conceptualization, Project administration, Data curation, Supervision, Validation. **Pablo Loma-Osorio:** Conceptualization, Data curation, Supervision, Validation. **Alexandra Pons Riverola:** Conceptualization, Data curation, Supervision, Validation. **Gil Bonet Pineda:** Conceptualization, Data curation, Supervision, Validation. **Nabil El Ouaddi:** Conceptualization, Data curation, Supervision, Validation. **Jaime Aboal:** Conceptualization, Data curation, Supervision, Validation. **Albert Ariza Solé:** Conceptualization, Data curation, Supervision, Validation. **Claudia Scardino:** Conceptualization, Data curation, Supervision, Validation. **Cosme García-García:** Conceptualization, Data curation, Supervision, Validation. **Estefanía Fernández-Peregrina:** Conceptualization, Project administration, Visualization, Writing – original draft, Writing – review & editing. **Alessandro Sionis:** Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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