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Characteristics, management, and mid-term prognosis of older adults with cardiogenic shock admitted to intensive care units: Insights from the FRENSHOCK registry

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Abbreviations:

ACE, angiotensin-converting enzyme; aHR, adjusted hazard ratio; AMI, acute myocardial infarction; aMCS, acute mechanical circulatory support; aOR, adjusted odds ratio; BNP, Brain natriuretic peptide; CI, confidence interval; CKD, chronic kidney disease; CS, cardiogenic shock; CVD, cardiovascular disease; DBP, diastolic blood pressure; ECLS, extracorporeal life support; GDMT, Guideline-directed medical therapy; GFR, glomerular filtration rate; HF, heart failure; HR, hazard ratio; HTx, heart transplantation; IABP, intra-aortic balloon pump; ICU, intensive care unit; ICCU, intensive cardiac care unit; ICD, implantable cardioverter-defibrillator; IQR, interquartile range; LVEF, left ventricle ejection fraction; MBP, mean blood pressure; NYHA, New York Heart Association; OP, older patients; PCI, percutaneous coronary intervention; PSVtdi, peak systolic velocity tissue Doppler imaging; PT, prothrombin time; RRT, renal replacement therapy; SBP, systolic blood pressure; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion; VAD, ventricular assist device.

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Cardiogenic shock Older adults Epidemiology Prognosis Mortality --

ABSTRACT

Background:

The incidence of heart failure and cardiogenic shock (CS) in older adults is continually increasing due to population aging. To date, prospective data detailing the specific characteristics, management and outcomes of CS in this population are scarce.

Methods:

FRENSHOCK is a prospective registry including 772 CS patients from 49 centers. We studied 1-month and 1-year mortality among patients over 75-year-old, adjusted for independent predictors of 1-month and 1-year mortalities.

Results:

Out of 772 patients included 236 (30.6%) were 75 years old or more (mean age 81.9 ± 4.7 years, 63.6% male). Compared to patients <75 years old, older adults had a higher prevalence of comorbidities including hypertension, dyslipidemia, chronic kidney disease, and history of heart disease. Older adults were characterized by a lower blood pressure, as well as higher creatinine and lower haemoglobin levels at presentation. Yet, they were less likely to be treated with norepinephrine, epinephrine, invasive ventilation, and renal replacement therapy. They showed a higher 1-month (aHR: 2.5 [1.86–3.35], $p < 0.01$) and 1-year mortality (aHR: 2.01 [1.58–2.56], $p < 0.01$). Analysis of both 1-month and 1-year mortality stratified by age quartiles showed a gradual relationship between aging and mortality in CS patients.

Conclusion:

A third of patient with CS in critical care unit are older than 75 years and their risk of death at one month and one year is more than double compared to the younger ones. Further research is essential to identify best therapeutic strategy in this population.

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1. Introduction

Heart failure (HF) and cardiogenic shock (CS) have an increasing incidence and now constitute one of the leading global causes of morbidity and mortality worldwide [1]. This is reinforced by the significant aging of the global population [2], which has transformed age-related healthcare into one of the most challenging domains of the 21st century [3]. As longevity extends and medical advances improves, the proportion of older patients within our population continues to grow, while age constitutes an unwavering risk factor for

cardiovascular diseases (CVD) [4], inevitably leading to a proportional increase in the number of patients suffering from HF [2,5]. As healthcare systems continue to improve, these conditions have become an all-too-common endpoint for many cardiac diseases, requiring further research and understanding [6,7].

Managing CS in older patients (OP) remains challenging: on the one hand, they more often present CS and severe forms, on the other their treatment options are restricted [8,9]. Indeed, the aggressive therapeutic interventions typically utilized in CS (mechanical circulatory support, renal replacement therapy) remain limited in the OP probably due to fear of harm (“*primum non nocere*”) and fear of futile treatment [10,11]. Ethical considerations often arise, questioning the balance between extending life and maintaining its quality [12]. Further, this population's vulnerability to complications, resulting from multiple comorbidities and physiological frailty, often limits the application of standard therapies [13].

Additionally, even though older individuals currently constitute a significant proportion of patients hospitalized for CS, they are nonetheless often underrepresented in clinical trials on this topic that often exclude patients above 75, 80 or 90 years [14,15]. This lack of representation impedes the development of appropriate personalized care for these patients.

This study aims to compare characteristics and outcomes of CS between patients 75 years or older and the younger patients, based on database from a large prospective multicentric registry of unselected CS. **2.**

Materials and methods

2.1. Patient population

As previously reported [16,17], FRENHOCK is a prospective, observational, and multicentre survey, conducted between April and October 2016, including 772 patients admitted for CS in ICU/ICCU in France, coming from various types of institutions (primary to tertiary centres, university and non-university, public and private hospitals)

All adult patients (≥ 18 years old) with CS were prospectively included in this registry if they met at least one criterion of each of the following three components: (1) Low cardiac output: low SBP < 90 mmHg and/or the need for maintenance with vasopressors/inotropes and/or a low cardiac index < 2.2 L/min/m²; (2) Left and/or right heart filling pressure elevation, defined by clinical signs, radiology, blood tests, echocardiography, or signs of invasive hemodynamic over IOPd and (3) Signs of organ malperfusion, which could be clinical (oliguria, confusion, pale and/or cold extremities, mottled skin) and/or biological (lactate > 2 mmol/L, metabolic acidosis, renal failure, liver insufficiency).

OP subjects were defined as those aged 75 years or more based on previous published series [6,7]. Ischemic CS was defined by the presence of at least one hemodynamically significant culprit lesion on coronary angiography (stenosis, thrombosis).

2.2. Data collection

Data collecting protocol has already been presented elsewhere [16,17], including medical history, cardiovascular risk factors, previous treatments, clinical, biological, and echocardiographic parameters (at admission and at 24 h), and in-hospital CS management [inotropes/ vasopressors, mechanical ventilation, renal replacement therapy (RRT) and acute mechanical circulatory support (aMCS)].

For each patient, investigators had to specify one to three triggers among the following: ischemic (type 1 or 2 AMI), mechanical complications (valvular injury, ventricular septal defect), ventricular and supraventricular arrhythmia, severe bradycardia, iatrogenesis (medication induced), infections, non-observance of previous medication.

2.3. Outcomes

All-cause mortality was assessed at 1-month by local investigator and at 1-year by dedicated research technicians based at the French Society of Cardiology as previously described [16]. It constitutes respectively, our primary and secondary endpoints. Moreover, heart transplantation (HTx) and ventricular assist devices (VAD) were assessed at one year.

2.4. Ethics

The study was conducted in accordance with the Helsinki declaration and French law. Written consent was obtained for all patients. Recorded data and their storage were approved by the CCTIRS (French Health. Research Data Processing Advisory Committee) (n° 15.897) and the CNIL (French Data Protection Agency) (n° DR-2016-109).

2.5. Statistical analysis

Continuous variables are reported as means and standard deviation (SD) or medians and interquartile ranges (IQR) when appropriate. Categorical variables are described as frequencies and percentages. Comparisons were made using Mann Whitney non-parametric test for continuous variables and chi-square test or Fisher's exact test for categorical variables. Paired data were analysed with Wilcoxon signed-rank test.

The main analysis was a comparison of characteristics, management and outcomes between OP, defined as being 75 years or older, and the remaining younger population. Two sensitivity analyses were made, examining the above primary and secondary outcomes including only patients older than 80 and 85 years.

To find independent predictors for each outcome of interest, multivariate stepwise logistic regression analysis was performed. Based on previous publications [17], the covariates included in the model consisted of all baseline characteristics (age, sex ratio, body mass index (BMI), cardiovascular risk factors, comorbidities, previous NYHA, history of previous heart disease, medications, initial cardiac arrest, sinus rhythm), as well as treatment modalities (diuretics, norepinephrine, epinephrine, dobutamine, renal replacement therapy, aMCS,

invasive and non-invasive ventilation), CS' triggers (ischemic, mechanical complication, ventricular and supraventricular arrhythmias, infections, non-observance, iatrogenesis), and markers of CS severity (left ventricular ejection fraction (LVEF) $\leq 30\%$, lactates ≥ 4 mmol/L, eGFR ≤ 30 mL/min). First, the association of all these characteristics and each primary and secondary outcome was assessed using univariable logistic regression analyses. Then, all significant independent predictors (defined at the level of 0.1) were integrated in multivariable analyses for each outcome and backwards reduced to only significant characteristics ($p \leq 0.05$). Finally, these significant characteristics were incorporated in multivariable models as fixed covariates for each adjusted outcome analysis. The variance inflation factor was used to rule out multicollinearity among the variables. Primary and secondary outcome of all-cause mortality was assessed using Kaplan-Meier time-to-event analysis, and Cox proportional hazards models were used to determine the adjusted hazard ratio (HR), 95% CI and p values. HTx and VAD at 1-year are reported as their rate and their adjusted OR and 95% CI.

To discern the potential incremental association between age and mortality, we further stratified the entire cohort into quartiles based on age and evaluated mortality across these strata. Lastly, we undertook an additional comparison between individuals suffering from ischemic and non-ischemic CS within the OP cohort.

All tests were two-tailed. A value of $p \leq 0.05$ was accepted as statistically significant. Analyses were performed using R software (version 4.1.2 (2021/ 11/ 01)).

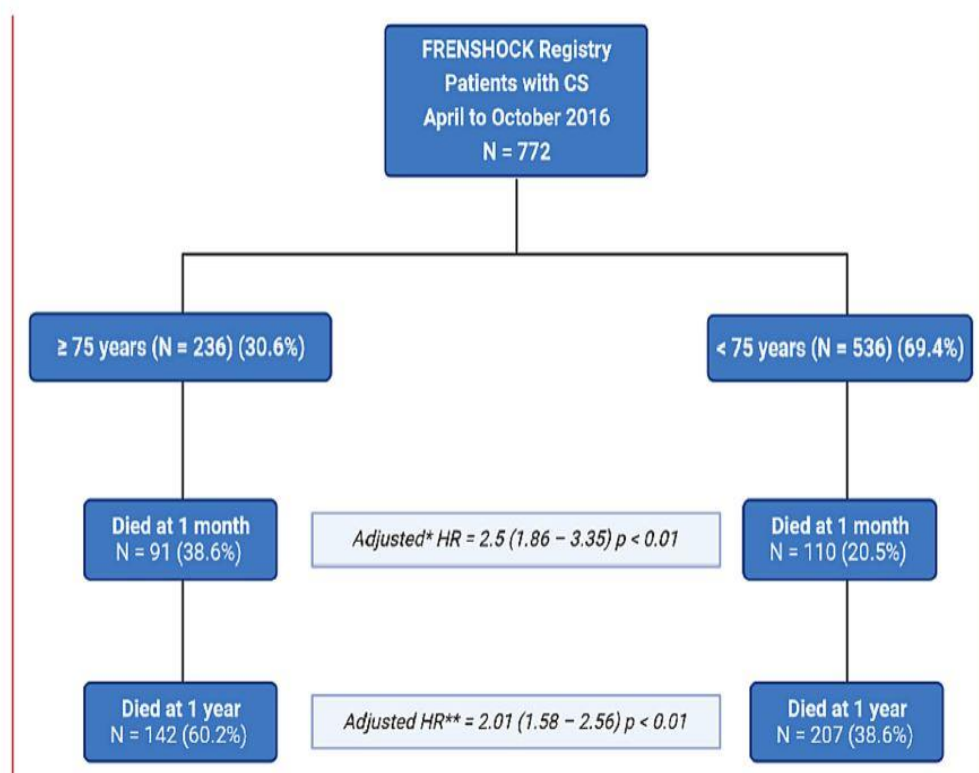


Fig. 1. Flow chart of the study.

Each adjusted outcome analysis included significant characteristics found as independent predictive factors in multivariable analyses and used as fixed covariates. CS = cardiogenic shock, HR = hazard ratio.

Table 1
Clinical characteristics, medical history, and usual medications at baseline according to age groups (< and ≥ 75 years).

	Overall population (n = 772)	≥ 75 years (n = 236)	< 75 years (n = 536)	p value
Age, mean ± SD	65.7 ± 14.9	81.9 ± 4.7	58.5 ± 11.9	< 0.01
Male, n (%)	552 (71.5)	150 (63.6)	402 (75)	< 0.01
Body mass index, mean ± SD, kg/m ²	25.8 ± 5.5 (n = 744)	25 ± 4.5 (n = 225)	26.2 ± 5.9 (n = 519)	0.02
Risk factors, n (%)				
Diabetes mellitus	217 (28.2) (n = 770)	71 (30.1)	146 (27.3) (n = 534)	0.49
Hypertension	364 (47.2) (n = 771)	161 (68.2)	203 (37.9) (n = 535)	< 0.01
Dyslipidemia	277 (35.9) (n = 771)	100 (42.4)	177 (33.1) (n = 535)	0.02
Current smoker	206 (27.8) (n = 740)	21 (9.4) (n = 224)	185 (35.9) (n = 516)	< 0.01
Medical history, n (%)				
Peripheral artery disease	91 (11.8) (n = 771)	33 (14)	58 (10.8) (n = 535)	0.26
Chronic kidney disease	164 (21.3) (n = 771)	81 (34.3)	83 (15.5) (n = 535)	< 0.01
COPD	50 (6.5) (n = 771)	21 (8.9)	29 (5.4) (n = 535)	0.1
ICD	127 (16.5) (n = 771)	24 (10.2)	103 (19.3) (n = 535)	< 0.01
Active cancer	51 (6.6) (n = 771)	18 (7.6)	33 (6.2) (n = 535)	0.55
Stroke	62 (8) (n = 771)	22 (9.3)	40 (7.5) (n = 535)	0.47
Previous NYHA functional status, n (%)				
≥ 3	295 (39.2) (n = 753)	100 (43.1) (n = 232)	195 (37.4) (n = 521)	0.16
History of cardiac disease, n (%)				
All causes	433 (56.1)	148 (62.7)	285 (53.3) (n = 535)	0.02
Ischemic	230 (29.8)	97 (41.1)	133 (24.8)	< 0.01
Hypertrophic	11 (1.4)	3 (1.3)	8 (1.5)	1
Toxic	34 (4.4)	4 (1.7)	30 (5.6)	0.02
Dilated	78 (10.1)	17 (7.2)	61 (11.4)	0.1
Valvular	65 (8.4)	31 (13.1)	34 (6.3)	< 0.01
Hypertensive	24 (3.1)	9 (3.8)	15 (2.8)	0.6
Previous medications, n (%)				
Aspirin	288 (37.4) (n = 770)	105 (44.4)	183 (34.3) (n = 534)	< 0.01
P2Y12 inhibitors	126 (16.4) (n = 770)	47 (19.9)	79 (14.8) (n = 534)	0.1
Vitamin K antagonist	165 (21.4) (n = 770)	66 (28)	99 (18.5) (n = 534)	< 0.01
Direct oral anticoagulant	56 (7.3) (n = 770)	17 (7.2)	39 (7.3) (n = 534)	1
Beta-blockers	316 (41) (n = 770)	106 (44.9)	210 (39.3) (n = 534)	0.17
ACE inhibitors	292 (37.9) (n = 770)	103 (43.6)	189 (35.4) (n = 534)	0.04
Sacubitril/valsartan	18 (2.5) (n = 727)	4 (1.8) (n = 220)	14 (2.8) (n = 507)	0.62
Statins	286 (37.1) (n = 770)	112 (47.5)	174 (32.6) (n = 534)	< 0.01
Loop diuretics	376 (48.8) (n = 770)	131 (55.5)	245 (45.9) (n = 534)	0.02
Aldosterone antagonist	108 (14) (n = 770)	24 (10.2)	84 (15.7) (n = 534)	0.053
Thiazide diuretics	45 (6) (n = 754)	19 (8.3) (n = 229)	26 (5) (n = 525)	0.11
Amiodarone	132 (17.6) (n = 752)	37 (16.4) (n = 225)	95 (18) (n = 527)	0.68

ACE = angiotensin-converting enzyme, CCB = calcium channel blocker, COPD = chronic obstructive pulmonary disease, CS = cardiogenic shock, ICD = implantable cardioverter-defibrillator, NYHA = New York Heart Association, SD = standard deviation.

3. Results

3.1. Baseline characteristics

Fig. 1 presents an overview of our study cohort: out of 772 CS patients incorporated from 49 centers, 236 (30.6%) were aged 75 or older, whose baseline characteristics are depicted in Table 1. The distribution of age groups within the cohort is provided in *Supplemental Fig. 1*. OP were more often females (36.4 vs 25%, $p < 0.01$), and exhibited a lower mean BMI (25.0 vs 26.2, $p = 0.02$), with higher rates of hypertension (68.2 vs 37.9%, $p < 0.01$), dyslipidaemia (42.4, 33.1%, $p = 0.02$) and chronic kidney disease (34.3 vs 15.5%, $p < 0.01$). In contrast, their smoking's prevalence was reduced (9.4 vs 35.9%, $p < 0.01$).

OP demonstrated a higher frequency of history of cardiac disease (62.7 vs 53.3%, $p = 0.02$), with an emphasis on ischemic (41.1 vs 24.8%, $p < 0.01$) and valvular (13.1 vs 6.3%, $p < 0.01$) cardiomyopathies, even though toxic heart disease was more prevalent in the younger group (1.7 vs 5.6%, $p = 0.02$). While the incidence of implantable cardioverter-defibrillator (ICD) was lower in the OP (10.2 vs 19.3%, $p < 0.01$), they were more commonly treated with ACE inhibitors (43.6 vs 35.4%, $p = 0.04$) and loop diuretics (55.5 vs 45.9%, $p = 0.02$).

No difference was found between the groups regarding CS triggers (*Supplementary Table 1*), with a predominance of ischemic (39.8 vs 34.7%, $p = 0.2$), supra-ventricular arrhythmias (11 vs 14.4%, $p = 0.25$), ventricular arrhythmias (9.7 vs 13.8%, $p = 0.15$), and infections (11 vs 12.3%, $p = 0.7$).

Significant associations between baseline characteristics and each outcome of interest can be found in *Supplementary table 2*.

3.2. CS presentation and evolution at 24 h according to age

Table 2 outlines the differences between both groups regarding clinical, biological, and echocardiographic parameters at admission and at 24 h. OP presented with lower blood pressure but without difference in terms of rate of HF signs and skin mottling. Biologically, OP presented with more elevated levels of creatinine (149.5 vs 124.0 $\mu\text{mol/L}$, $p < 0.01$) and Nt-proBNP (16,000 vs 6787 pg/mL, $p < 0.01$), whereas lactate levels remained consistent between groups (3.0 vs 3.0 mmol/L, $p = 0.49$). The echocardiographic evaluations showed a relatively higher LVEF (29.3 vs 25%, $p < 0.01$) in the OP group, notably including a greater proportion of patients with preserved LVEF ($\geq 50\%$) (11.9% vs 6.5%, $p = 0.02$), alongside an increased prevalence of aortic stenosis (9.6 vs 2.6%, $p < 0.01$).

3.3. In hospital management according to age

Table 3 underscores the variances in therapeutic approaches between groups. Dobutamine was the main inotrope used whatever the age group (80.9 vs 82.9%, $p = 0.58$) even though OP received less norepinephrine (47.9 vs 55.8%, $p = 0.05$) and epinephrine (7.2 vs 14.7%, $p < 0.01$). Loop diuretics (74.1 vs 64.4%, $p = 0.01$) were more routinely administered in OP. While no significant difference was observed between groups regarding the use of non-invasive ventilation, OP were less frequently subjected to various forms of organ support.

This includes invasive ventilation (24.6% vs 43.8%, $p < 0.01$), renal replacement therapy (9.3% vs 18.7%, $p < 0.01$), and acute mechanical circulatory support (aMCS) (6.4% vs 24%, $p < 0.01$). However, OP benefited more from percutaneous coronary intervention (PCI) (34.7% vs 27%, $p = 0.04$).

3.4. Short and long-term outcomes

An age of 75 years or older was associated with a significantly higher 1-month (38.6 vs 20.5%, aHR: 2.5 [1.86–3.35], $p < 0.01$) and 1-year all-causes mortality (60.2 vs 38.6%, aHR: 2.01 [1.58–2.56], $p < 0.01$), as shown in Fig. 2. Conversely, the 1-year recourse to VAD and/or HTx was lower for OP (3 vs 13.2%, aOR 0.36 [0.15–0.91], $p = 0.03$). No significant difference was found between ischemic and non-ischemic CS in the OP group (*Supplementary Fig. 2*). Additional analyses with age thresholds >80 and 85 years showed similar results, with higher 1-month and 1-year mortality, as well as a trend towards a lower number of VAD or HTx (*Supplementary Fig. 3 & 4, Supplementary Table 3*). Fig. 3 shows that, based on quartiles subdivision, it exists a graded relationship between age and mortality, demonstrating a proportional increase in mortality as age escalates, with a significant cut-off starting from the age of 66 for 1-month mortality, and 58 for 1-year mortality.

3.5. ICU-related complications

No difference was reported regarding the most common complications, whether for ischemic (3.2 vs 4.1%, $p = 0.69$) or hemorrhagic (0.9 vs 1.4%, $p = 0.73$) strokes, gastrointestinal bleeding (4.1 vs 4.1%, $p = 1$), pneumonia (16.1 vs 21.4%, $p = 0.12$) and urinary (4.9 vs 3.7%, $p = 0.59$), or bloodstream (11.2 vs 14.3%, $p = 0.29$) infections. However, it is worth noting a higher incidence of pericardial effusion in the cohort of younger patients (0 vs 2.2%, $p = 0.04$) (*Supplementary Table 4*).

4. Discussion

Within this prospective, multicentre study including 772 CS patients with unselected aetiology managed in routine practice, OP patients (≥ 75 years old) constituted almost one-third of the population, affected by more comorbidities (heart failure, chronic kidney disease), and treated less invasively (lower rate of norepinephrine, epinephrine, RRT and aMCS use). We observed a strong, independent, and graded relationship between older age and both lower 1-month and 1-year survival.

The OP constituted one third of the patients in this study, which seems consistent with prior recent CS studies [18,19]. There was no difference in the distribution of CS triggers among age groups, with ischemic aetiology being the most prevalent at about 35–40%. This proportion is lower than reported in older studies, where ischemic aetiology typically accounts for around 70–80% [6,7], likely related to the varied care settings included in our study, spanning from primary to tertiary centers, as well as both university and non-university hospitals, and private institutions. So, although ischemic cause remains the most common individual trigger of CS, non-ischemic causes collectively outweighed it in terms of frequency, underlying the growing awareness regarding non-ischemic CS, which, while

predominant in everyday practice, remain underrepresented in previous publications [20]. Our findings did not demonstrate any difference in prognosis between ischemic and non-ischemic CS in the specific OP as we previously found in the general FRENDSHOCK population analysis [17]. Possible explanation could be the absence of collection of other geriatric factors that may override this difference such as the degree of dependence or frailty before hospitalization. Nevertheless, data on general population comparing prognosis in ischemic and non-ischemic CS remains conflicting [21–23]. A reassuring point is the PCI rate in the OP group, approaching 35% as in the younger cohort, which is coherent with previous studies indicating the benefit of myocardial revascularization even for OP [19,24].

Older age is already known as a strong risk factor for mortality whatever the pathology or condition studied including among patients with CS [6,7,25], illustrated by an odds ratio of 1.06 per additional year of age for 1-month mortality in our previous analysis [17]. This study confirms a gradual association between age and CS mortality with an emphasis for patients aged 75 years and older and extends this prognostic decline to non-ischemic CS, which constitutes most cases in our cohort. In addition, our quartile analysis revealed that mortality began to significantly increase from the age of 66 years for 1-month mortality and 58 years for 1-year mortality, consistent with prior studies that have identified age cut-offs ranging from ≥ 65 to >75 years for prediction of higher mortality among patients with CS [6,7].

This observed excess mortality in older subjects is undoubtedly explained by various age-related factors hindering their response capabilities to the hemodynamic stresses of CS, such as frailty, lower access to admissions or reluctance, cellular aging, atypical clinical presentation, multimorbidity, altered drug metabolism or reduced functional reserve [3,26]. Otherwise, in our study, the initial clinical presentation of the OP cohort seemed slightly more severe than younger patients, with more comorbidities, lower blood pressure and more pronounced renal impairment, although the higher prevalence of CKD at baseline must be considered.

Despite their more severe presentation, older subjects were less frequently treated with norepinephrine, renal replacement therapy, invasive ventilation and aMCS suggesting potential limitations on the aggressiveness of care in the setting of critical illness and a poor anticipated prognosis in this population. This remark underlines the interest of our real-life approach as this population remains underrepresented in classical trials.

Meanwhile, even if older patients had more comorbidities, worse kidney function, and decreased use of MCS devices, they had a significantly higher risk of mortality despite adjusting for these factors in addition to shock severity.

Moreover, while advanced therapies for CS provide encouraging results, they often come with a high risk of complications that increase with age and is negatively associated with outcomes [27], which may discourage physicians from using them. However, even though age is not a contraindication per se to the use of such treatments, patients who might benefit from them should be carefully selected, considering their general condition before CS, frailty criteria, and expected chances of recovery [28].

Table 2

Clinical, echocardiographic, and biological findings at baseline according to age groups (< and ≥ 75 years).

	Overall population (n = 772)	≥ 75 years (n = 236)	< 75 years (n = 536)	p value
Clinical presentation at admission				
Heart rate, mean ± SD, bpm	95.6 ± 29.6 (n = 769)	92.2 ± 28.1 (n = 235)	97.2 ± 30.1 (n = 534)	0.04
SBP, mean ± SD, mmHg	101.2 ± 25.2 (n = 770)	101.7 ± 27	101 ± 24.3 (n = 534)	0.63
DBP, mean ± SD, mmHg	63.2 ± 17.4 (n = 769)	60.5 ± 17.5 (n = 235)	64.4 ± 17.2 (n = 534)	< 0.01
MBP, mean ± SD, mmHg	74.9 ± 18.3 (n = 767)	72.9 ± 18 (n = 235)	75.8 ± 18.4 (n = 532)	0.02
Sinus rhythm, n (%)	399 (52) (n = 768)	90 (41.5)	301 (56.6) (n = 532)	< 0.01
Motting, n (%)	256 (38.8) (n = 660)	73 (34.6) (n = 211)	183 (40.8) (n = 449)	0.15
Left heart failure, n (%)	554 (71.9) (n = 770)	165 (69.9)	389 (72.8) (n = 534)	0.45
Right heart failure, n (%)	377 (49.1) (n = 768)	123 (52.3) (n = 235)	254 (47.7) (n = 533)	0.26
Cardiac arrest, n (%)	79 (10.2) (n = 771)	19 (8.1)	60 (11.2) (n = 535)	0.23
Blood tests at admission, median (IQR)				
Sodium, mmol/L				
Potassium, mmol/L	135 (132–139) (n = 760)	136 (133–138.8) (n = 234)	135 (131–138) (n = 526)	< 0.01
Creatinine, μmol/L	4 (4–5) (n = 638)	4 (4–5) (n = 194)	4 (4–5) (n = 444)	0.78
Bilirubin, mg/L	133 (96–190) (n = 761)	149.5 (112.3–210) (n = 234)	124 (90–169.5) (n = 527)	< 0.01
Haemoglobin, g/dL	16 (9–29) (n = 544)	16 (9–29) (n = 169)	16 (9.5–30) (n = 375)	0.34
Arterial blood lactates, mmol/L	12.6 (11–14) (n = 754)	12 (11–13.9) (n = 233)	13 (11–14.2) (n = 521)	< 0.01
ASAT, UI/L	3 (2–4.7) (n = 684)	3 (2–4) (n = 210)	3 (2–5) (n = 474)	0.49
ALAT, UI/L	90 (39–299.5) (n = 547)	115 (41–396.5) (n = 164)	83 (38–277) (n = 383)	0.11
PT, %	59 (27–182.5) (n = 559)	56 (24–167.5) (n = 170)	60 (28–184) (n = 389)	0.47
Nt-proBNP, pg/mL	59 (37–77) (n = 731)	57 (33–77) (n = 225)	59 (39–77) (n = 506)	0.21
BNP, pg/mL	9276.5 (4057.8–22,702.5) (n = 224)	16,000 (8240–35,000) (n = 65)	6787 (3629–15,499.5) (n = 159)	< 0.01
CRP, mg/L	1150 (476.8–2757.3) (n = 264)	1233 (638.5–3602.5) (n = 103)	1105 (410–2466) (n = 161)	0.02
Baseline echocardiography				
LVEF, mean ± SD, %	28 (9–69) (n = 406)	32 (12–65) (n = 137)	27 (8–71) (n = 269)	0.31
TAPSE, median (IQR), mm	26.3 ± 13.4 (n = 763)	29.3 ± 13.6 (n = 231)	25 ± 13 (n = 532)	< 0.01
PSVtdi, median (IQR), cm/s	13 (10–16) (n = 259)	14 (10–16) (n = 69)	13 (10–16.8) (n = 190)	0.93
Severe mitral regurgitation, n (%)	8 (6–11) (n = 206)	8 (6.5–10) (n = 55)	8 (6–11) (n = 151)	0.91
Severe aortic stenosis, n (%)	107 (14.6) (n = 733)	30 (13.6) (n = 221)	77 (15) (n = 512)	0.69
Severe aortic regurgitation, n (%)	36 (4.7) (n = 759)	22 (9.6) (n = 229)	14 (2.6) (n = 530)	< 0.01
	10 (1.3) (n = 755)	3 (1.3) (n = 225)	7 (1.3) (n = 530)	1

ALAT = alanine aminotransferase, ASAT = aspartate aminotransferase, BNP = Brain natriuretic peptide, CRP = C-reactive protein, DBP = diastolic blood pressure, IQR = interquartile range, LVEF = left ventricular ejection fraction, MBP = mean blood pressure, Nt-proBNP = N-terminal-pro hormone BNP, PSVtdi = peak systolic velocity tissue Doppler imaging, PT = prothrombin time, SBP = systolic blood pressure, SD = standard deviation, TAPSE = tricuspid annular plane systolic excursion.

Nevertheless, it is uncertain whether the higher mortality observed in the OP group is only age-related or secondary to others unconsidered factors whether related to the patient (other comorbidities, dependence, or frailty for example), or to the physician (age-related differences in history taking, shock recognition, diagnostic testing, or treatment implementation). Since they benefited from less invasive management and they die twice, inequalities in the quality of care should be questioned. Besides, unlike younger patients, some advanced heart failure treatments such as chronic VAD and HTx may seem unreasonable especially in this CS context. Instead, the management plan should focus on optimizing medical treatment and implementing GDMT. Remote monitoring also presents a compelling approach for early detection of HF recurrences and the corresponding adjustment of medication treatments [29], aiming to enhance quality of life, which remains the primary objective to achieve.

All these findings underline the frequency, severity, and complexity of managing CS in OP, with both short- and long-term prognoses appearing to be encumbered, highlighting the importance of global evaluation of the patient considering not only age but dependence and frailty, to avoid potential ethical dilemmas. As a result, to provide the most thorough and individualized care, the management of these patients should be more extensively discussed within multidisciplinary teams involving geriatrician, intensivist and cardiologist, ideally within the framework of geriatric intensive care units, representing an interesting future perspective given the expectation of facing increasingly critical situations with OP patients.

Table 3
In-hospital management according to age groups (< and ≥ 75 years).

	Overall population (n = 772)	≥ 75 years (n = 236)	< 75 years (n = 536)	p value
Medications used, n (%)				
Dobutamine	632 (82.3) (n = 768)	191 (80.9)	441 (82.9) (n = 532)	0.58
Norepinephrine	410 (53.4) (n = 768)	113 (47.9)	297 (55.8) (n = 532)	0.0502
Epinephrine	95 (12.4) (n = 768)	17 (7.2)	78 (14.7) (n = 532)	< 0.01
Levosimendan	57 (7.4) (n = 768)	13 (5.5)	44 (8.3) (n = 532)	0.23
Loop diuretics	467 (67.4) (n = 693)	160 (74.1) (n = 216)	307 (64.4) (n = 477)	0.01
Thiazide diuretics	27 (4) (n = 682)	12 (5.7) (n = 212)	15 (3.2) (n = 470)	0.19
Aldosterone antagonist	91 (13.1) (n = 693)	24 (11.1) (n = 216)	67 (14) (n = 477)	0.35
Respiratory support, n (%)				
Non-invasive	199 (25.9) (n = 768)	71 (30.1)	128 (24.1) (n = 532)	0.1
Invasive	291 (37.9) (n = 768)	58 (24.6)	233 (43.8) (n = 532)	< 0.01
Short-term mechanical circulatory support, n (%)				
Overall	143 (18.6) (n = 770)	15 (6.4)	128 (24) (n = 534)	< 0.01
IABP	48 (6.2) (n = 770)	12 (5.1)	36 (6.7) (n = 534)	0.47
Impella	26 (3.4) (n = 770)	0 (0)	26 (4.9) (n = 534)	< 0.01
ECLS	85 (11) (n = 770)	4 (1.7)	81 (15.2) (n = 534)	< 0.01
Renal replacement therapy, n (%)				
Any PCI, n (%)	226 (29.4) (n = 769)	82 (34.7)	144 (27) (n = 533)	0.04

CS = cardiogenic shock, ECLS = extracorporeal life support, IABP = intra-aortic balloon pump, PCI = percutaneous coronary intervention.

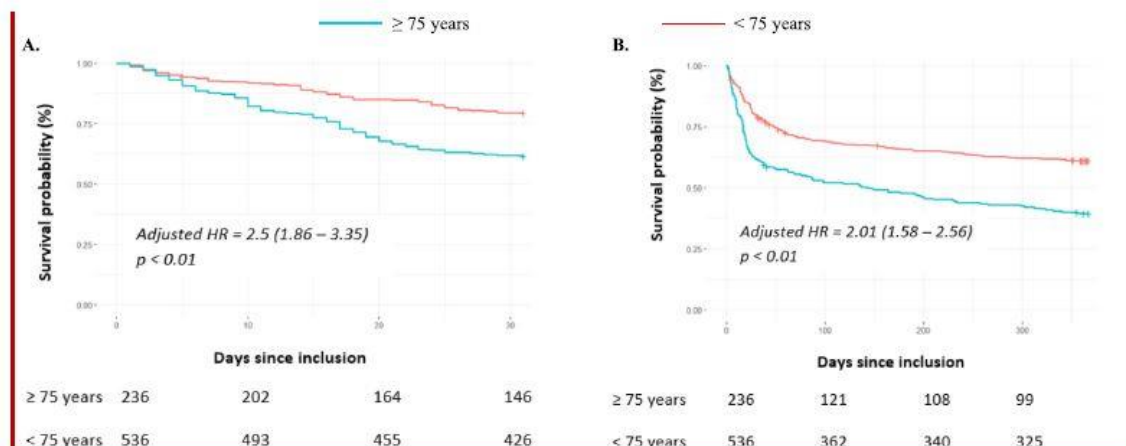


Fig. 2. Short- and long-term mortality outcomes after CS according to age.

Panel A represents 1-month overall mortality. Panel B focuses on 1-year mortality. The cumulative incidences of 1-year and 1-month mortality were estimated using the Kaplan-Meier method; hazard ratios and 95% confidence intervals were estimated using Cox regression models.

According to significant characteristics found to be independent predictive factors in multivariable analyses, 1-year mortality was adjusted for BMI ≥ 25, chronic kidney disease, active cancer, history of ischemic cardiomyopathy, any PCI, use of norepinephrine, renal replacement therapy, aMCS, non-observance trigger, and sinus rhythm. 1-month mortality was adjusted for chronic kidney disease, use of norepinephrine, renal replacement therapy, LVEF < 30%, and infectious trigger. CS = cardiogenic shock, HR = hazard ratio.

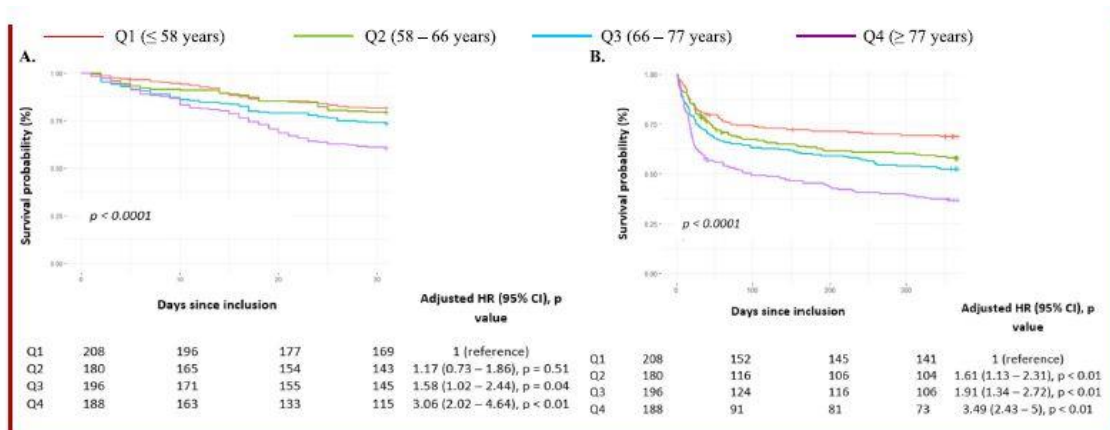


Fig. 3. Short- and long-term mortality outcomes after CS stratified by age quartiles.

Panel A represents 1-month overall mortality. Panel B focuses on 1-year mortality. The cumulative incidences of 1-year and 1-month mortality were estimated using the Kaplan–Meier method; hazard ratios and 95% confidence intervals were estimated using Cox regression models.

According to significant characteristics found to be independent predictive factors in multivariable analyses, 1-year mortality was adjusted for BMI ≥ 25 , chronic kidney disease, active cancer, history of ischemic cardiomyopathy, any PCI, use of norepinephrine, renal replacement therapy, aMCS, non-observance trigger, and sinus rhythm. 1-month mortality was adjusted for chronic kidney disease, use of norepinephrine, renal replacement therapy, LVEF $\leq 30\%$, and infectious trigger. CS = cardiogenic shock, HR = hazard ratio.

5. Limitations

The main limitation is the lack of data regarding the geriatric assessment of the general and functional status, including frailty criteria or comorbidity score (such as Charlson Comorbidity Index) which would have allowed for a study stratified by frailty group to assess the potential benefit of more aggressive treatment in the most robust older subjects. Future studies should endeavor to collect this data to improve the management of elderly and very elderly patients in the future. Similarly, we also did not have information regarding established care limitations, such as “not to be resuscitated” orders, or transitions to palliative care, which would have likewise allowed a more nuanced study of prognosis according to the degree of robustness. Besides mortality, it would also be pertinent to examine the changes in functional capacities before and after CS, and the prospects for medium-term recovery

It is noteworthy that there was a higher prevalence of preserved LVEF among those aged 75 and over, possible owing to a higher occurrence of specific cardiac conditions like cardiac amyloidosis, relatively frequent among the elderly, but also frequently underdiagnosed [30]. As our cohort's data traces back to 2016, a time when the understanding and detection of amyloidosis were less advanced, we lack sufficient data to properly address this issue.

Another notable limitation is the year of our data collection, which dates back to 2016. The concern arising from this temporal gap is understood, especially in rapidly evolving fields. However, this dataset, despite its age, captures a distinctive and realistic snapshot of the clinical practices and patient demographic characteristics prevalent at that time. Subsequent studies, when juxtaposed against this dataset, stand to gain a more nuanced understanding, allowing researchers to discern intricate trends, evolutions in treatment modalities, and demographic shifts over the ensuing years.

As previously described [16,17], the FRENDSHOCK registry targeted patients from ICU and ICCU, either admitted directly or post-transfer from another centre. Consequently, we cannot rule out the possibility that individuals with severe comorbidities, advanced age, or extensive

multi-organ failure might not have been transferred due to perceived futility. Additionally, our data collection did not include those who succumbed early, specifically patients who died before informed consent could be obtained, leading to a potential underestimation of mortality within our cohort. Nevertheless, the representativeness of our dataset is still reasonably acceptable, as underscored by the fact that over a third of our studied population was aged 75 years or above, >8% exceeded 85 years of age, and the eldest participant was 98 years old. Finally, we were not able to use the SCAI SHOCK Stage Classification given that it was not yet available at the time of our study.

6. Conclusion

A third of CS patients in the intensive care unit are over 75 years old. Although their risk of death at one month and one year is more than doubled compared to the youngest, they benefited less from invasive management, raising the question of the therapeutic choices made in this population. Further research is essential to identify best therapeutic strategy in this population.

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Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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