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Hemoglobin in cardiogenic shock: the lower, the poorer survival

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Abstract

Background Cardiogenic shock (CS) is a severe hemodynamic condition with high mortality. Although extremely frequent in daily practice, the impact of anemia in CS is largely unknown. This study focuses on the consequences of low hemoglobin (Hb) level on the outcomes of CS patients.

Methods FRENSHOCK is a prospective registry including 772 CS patients from 49 centers. One-month and one-year mortalities were analyzed according to the admission level of Hb.

Results Among 754 patients, 71.8% were male, with a mean age of 65.8 (± 14.8) years, and 361 (47.9%) presenting with anemia. Four groups were defined, depending on admission Hb levels by quartiles: Q1: Hb < 11.0 g/dL, Q2: Hb 11–12.6 g/dL, Q3: Hb > 12.6–14 g/dL, and Q4: Hb > 14.0 g/dL. Patients from the Q1 group required more frequent renal replacement therapy and norepinephrine. A significant increase in all-cause mortality was observed across Hb quartiles at 1 month (Ptrend = 0.035) and 1 year (Ptrend < 0.01). Q1 patients had 1.64 times higher mortality at 1 month (1.09–2.47, p = 0.02) and 2.53 times higher mortality at 1 year (1.84–3.49, p < 0.01) compared to Q4. The negative effect of low Hb level was confirmed in multivariate Cox regression adjusted for baseline characteristics, and was stronger in men, non-ischemic CS, patients without CKD and patients aged < 67 years.

Conclusion Anemia is a common condition frequently intertwined with CS worsening both short- and long-term mortality. Further randomized studies are warranted to understand its mechanisms and adapt the transfusion strategy.

Keywords Cardiogenic shock, Anemia, Hemoglobin, Prognosis, Mortality

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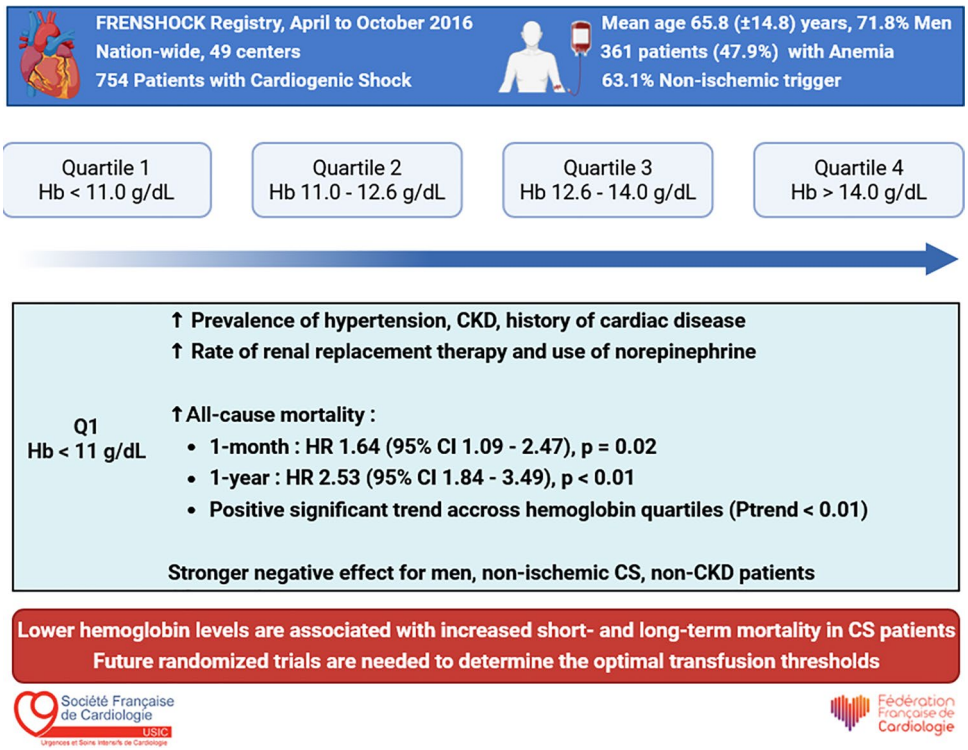
Graphical Abstract



Introduction

Cardiogenic shock (CS) is a life-threatening hemodynamic condition due to primary cardiac dysfunction resulting in an inadequate cardiac output which can result in multi-organ failure and death [1]. Despite improved pharmacologic and device-based therapies, CS mortality remains unacceptably high, approaching 25–30% [2] at 1 month and 45–60% at 1 year [3]. Its optimal management still lacks a clear consensus regarding best practices [4], and several blind spots continue to be a matter of debate, particularly in the management of associated comorbidities.

In this regard, anemia represents both a factor in the genesis and maintenance of hemodynamic instability, leading to reduced oxygen tissue delivery, impaired oxygen utilization, and chronic tissue ischemia [5]. Its detrimental impact in chronic heart failure (HF) is now well documented, particularly through iron deficiency, which exerts a negative effect on oxygen metabolism in cardiac and peripheral tissues [1]. Moreover, anemia is a very common phenomenon, especially among critically ill patients: by day 3 after admission in intensive care unit (ICU), almost 95% of patients are anemic (i.e., hemoglobin < 13 g/dl in men and < 12 g/dl in women), and anemia persists throughout their ICU and hospital stay, with or without red blood cell (RBC) transfusion [6]. The etiology of anemia in the ICU can be multifactorial, involving to varying degrees hemodilution, nutritional deficiencies, acute hemorrhage, acute inflammation, and functional iron deficiency [5–7].

Despite this association between high prevalence and significant potential harm, data regarding the specific management of anemia in CS remain scarce, with no randomized controlled trials (RCT) conducted to date. Yet, guidelines for RBC transfusion have identified patients with cardiovascular disease as a population in need of more prospective data [7]. This has led to multiple RCTs in the context of acute myocardial infarction (AMI), without CS, where the overall data seem to converge on the absence of differences in mortality outcomes between liberal and restrictive RBC transfusion strategies [8, 9]. Whether this assumption holds true in the context of CS remains uncertain, given that it represents a more advanced stage in terms of metabolic demand and peripheral hypoperfusion. Indeed, the limited existing data, mainly focused on CS complicating AMI (AMI-CS), appear to establish a clear association between anemia and a higher risk of death from any cause or the need

for renal replacement therapy (RRT) within 30 days after hospitalization [5]. However, mounting evidence suggests that the epidemiological profile of CS is shifting towards a predominance of non-ischemic CS (NICS), primarily due to the natural progression of HF [4], in which little is known about the impact and treatment of anemia.

Hence, the present study aimed to assess the association between anemia and all-cause mortality in a contemporary cohort of unselected CS patients with a broad range of etiologies.

Material and methods

Patient population

As previously reported [2, 10], FRENSHOCK is a prospective, observational, and multicenter 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 centers, universities, 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/m^2; (2) Left and/or right heart filling pressure elevation, defined by clinical signs, radiology, blood tests, echocardiography, or signs of invasive hemodynamic overload 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).

Each patient had up to three identified triggers for CS determined by the local investigator, classified as ischemic (Type 1 or Type 2 AMI following European guidelines), ventricular and supraventricular arrhythmia, conduction disorder, infectious disease, non-compliance (inadequate adherence to medical treatment or hygiene and diet rules, such as stopping or skipping an angiotensin-converting enzyme inhibitor or beta-blocker treatment, deviation from a low sodium diet, etc.), or iatrogenesis.

Data collection

The data collection protocol has been previously published elsewhere [2, 10, 11]. In brief, the data acquisition process encompassed the gathering of comprehensive medical history, previous treatments, in-hospital CS management [inotropes/vasopressors, mechanical ventilation, and acute mechanical circulatory support (aMCS)], clinical, biological, and echocardiographic parameters (at admission and at 24 h). Anemia was classified in accordance with the World Health Organization definitions: hemoglobin (Hb) < 13 g/dl in men and < 12 g/dl in women. The reported hemoglobin level is the one obtained at inclusion, on the first day of management. Any transfusions performed occurred after the baseline hemoglobin value was obtained, according to local protocols. The follow-up was conducted at 30 days by the local investigator and at 1 year by dedicated research technicians from the French Society of Cardiology.

Unfortunately, the SCAI SHOCK Stage Classification [12] was not yet available at the time of our study, which is why this data could not be prospectively collected. However, by relying on the method previously described by Thayer et al. [13], we were able to retrospectively determine the maximum SCAI classification stage reached during hospitalization based on the total use of vasopressors, inotropes, and aMCS devices.

Endpoints

All-cause mortality was assessed at one month and one year. The primary endpoint was 1-month all-cause mortality. Secondary endpoint was 1-year all-cause mortality.

Statistical analysis

Continuous variables were reported as means and standard deviation (SD) or medians and interquartile ranges (IQR) when appropriate. Categorical variables were described as frequencies and percentages. The overall population was divided into quartiles based on the basal level of Hb. Quantitative variables were compared by the Kruskal–Wallis test. Categorical variables were compared by the Pearson chi-square test or, when indicated, the Fisher exact test. To analyze trends across quartiles, we employed the Cochran-Armitage test for qualitative variables and the Jonckheere-Terpstra test for quantitative variables, both described in the text and tables as "Ptrend". 'Additionally, a multivariable Cox regression model was performed to assess the relationship between all-cause mortality and several covariates, including Hb level, along with various clinical and biological factors available at hospital presentation, and variables related to initial treatment. These covariates were selected based on their clinical and pathophysiological relevance, according to Prognosis Research Strategy guidelines [14], which recommend a clinically hypothesis-driven approach for a priori selection of all model variables, as opposed to bivariate association testing methods. Kaplan–Meier time-to-event curves for 1-month and 1-year all-cause mortality were used to compare mortality rates across quartile groups. Differences between groups were assessed using the log-rank test, and hazard ratios (HRs) were computed

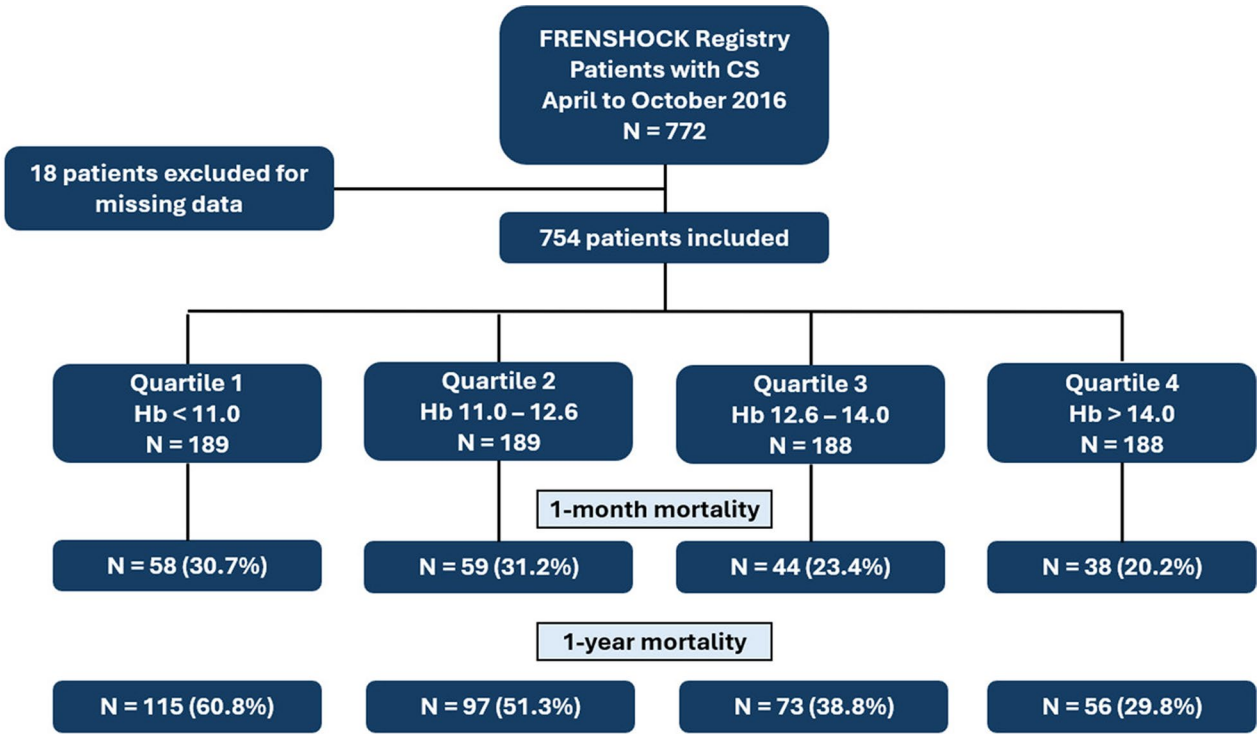


Fig. 1 Flow chart of the study. *CS* cardiogenic shock

through Cox regression. No imputation was applied for missing data. A multivariate logistic regression analysis was performed as a sensitivity analysis to assess the association between hemoglobin and all-cause mortality at 30 days and 1 year using the same covariates, with results presented as adjusted odds ratios (aOR) with 95% CIs. In addition, a Cox model with 3-knots restricted cubic spline (RCS) functions and threshold effects was performed in the overall population to determine the optimal predictive cut-off point for Hb and to assess the shape of the associations between Hb levels (as a continuous measure) and all-cause mortality. Potential nonlinearity was evaluated using a likelihood ratio test, comparing the model with only a linear term to the model including both linear and cubic spline terms. Eventually, based on the gaps identified in the literature and pathophysiological considerations [7–9], we conducted prespecified subgroup analyses to evaluate the differential impact of Hb levels according to sex, history of chronic kidney disease (CKD), the ischemic or non-ischemic trigger of CS, and age (with a threshold set at 67 years, the median of the 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 4.3.2 (2023-10-31)].

Results

Baseline patients' characteristics

As represented in Fig. 1, this analysis included 754 CS patients from a total of 49 centers (18 patients excluded for missing Hb level at admission). In accordance with the World Health Organization thresholds, 361 patients (47.9%) presented with anemia at initial admission, including 253 male individuals and 108 female individuals (Hb levels < 13 g/dL and 12 g/dL, respectively). Patients were categorized into four quartiles based on their Hb level at admission: Quartile 1 (Q1) group with a Hb < 11.0 g/dL, Quartile 2 (Q2) group with Hb levels ranging from 11.0 to 12.6 g/dL, Quartile (Q3) group with Hb levels ranging from > 12.6 to 14.0 g/dL, and Quartile (Q4) with Hb > 14.0 g/dL (overall hemoglobin level distribution described as a histogram in Supplementary Fig. 1).

Table 1 provides a comprehensive overview of the baseline characteristics of the study cohort. The mean age was 65.8 (± 14.8) years, with predominance of men (71.8%). Patients in the lowest Hb quartile (Q1) were older ($p < 0.01$), more frequently male ($p < 0.01$), and had a lower body mass index ($p < 0.01$), all demonstrating a significant trend across quartiles. They also exhibited a higher prevalence of comorbidities, including hypertension ($p < 0.01$), CKD (< 0.01), and active cancer (< 0.01), with a similarly increasing trend observed across quartiles (Ptrend < 0.01). Furthermore, these patients more

Table 1 Baseline characteristics according to hemoglobin level on the first day of management

	Overall population (n = 754)	Quartile 1 (< 11.0) (n = 189)	Quartile 2 (11.0–12.6) (n = 189)	Quartile 3 (12.6–14.0) (n = 188)	Quartile 4 (14.1–21.7) (n = 188)	p value	P_{trend}
Age, mean ± SD, years	65.8 ± 14.8	67.7 ± 14.2	67.0 ± 15.3	66.9 ± 14.6	61.6 ± 14.5	< 0.01	< 0.01
Male sex, n (%)	541 (71.8)	108 (57.1)	132 (69.8)	140 (74.5)	161 (85.2)	< 0.01	< 0.01
Body mass index, mean ± SD, kg/m^2	25.8 ± 5.5 (n = 729)	25.5 ± 5.6 (n = 182)	25.0 ± 5.7 (n = 182)	26.7 ± 5.5 (n = 183)	26.1 ± 5.1 (n = 182)	< 0.01	0.03
Risk factors, n (%)							
Diabetes mellitus	212 (28.2) (n = 753)	60 (31.7)	54 (28.6)	56 (29.9) (n = 187)	42 (22.3)	0.20	0.07
Hypertension	358 (47.5)	107 (56.6)	94 (49.7)	88 (46.8)	69 (36.7)	< 0.01	< 0.01
Dyslipidemia	271 (35.9)	76 (40.2)	73 (38.6)	68 (36.2)	54 (28.7)	0.10	0.02
Current smoker	201 (27.8) (n = 722)	44 (24.3) (n = 181)	46 (26.0) (n = 177)	36 (19.8) (n = 182)	75 (41.2) (n = 182)	< 0.01	< 0.01
Medical history, n (%)							
Peripheral artery disease	90 (12.0) (n = 753)	22 (11.6)	30 (15.9)	20 (10.6)	18 (9.6) (n = 187)	0.26	0.29
Chronic kidney disease	160 (21.2) (n = 753)	58 (30.7)	51 (27.0)	32 (17.0)	19 (10.2) (n = 187)	< 0.01	< 0.01
COPD	50 (6.6) (n = 753)	16 (8.5)	13 (6.9)	12 (6.4)	9 (4.8) (n = 187)	0.56	0.16
ICD	123 (16.3) (n = 753)	32 (16.9)	43 (22.8)	26 (13.8)	22 (11.8) (n = 187)	0.02	0.04
Active cancer	51 (6.8) (n = 753)	23 (12.2)	16 (8.5)	8 (4.3)	4 (2.1) (n = 187)	< 0.01	< 0.01
Stroke	60 (8.0) (n = 753)	20 (10.6)	19 (10.1)	11 (5.9)	10 (5.3) (n = 187)	0.13	0.02
Previous PCI	162 (21.5) (n = 753)	49 (25.9)	46 (24.3)	38 (20.2)	29 (15.5) (n = 187)	0.06	< 0.01
NYHA functional status, n (%)							
≥ 3	289 (39.2) (n = 738)	76 (41.8) (n = 182)	82 (43.6) (n = 188)	61 (32.8) (n = 186)	70 (38.5) (n = 182)	0.15	0.20
History of cardiac disease, n (%)							
All causes	424 (56.2)	119 (63.0)	122 (64.6)	96 (51.1)	87 (46.3)	< 0.01	< 0.01
Ischemic	226 (30.0)	69 (36.5)	69 (36.5)	50 (26.6)	38 (20.2)		
Hypertrophic	11 (1.5)	1 (0.5)	3 (1.6)	2 (1.1)	5 (2.7)		
Toxic	34 (4.5)	5 (2.6)	10 (5.3)	4 (2.1)	15 (8.0)		
Dilated	77 (10.2)	15 (7.9)	17 (9.0)	25 (13.3)	20 (10.6)		
Valvular	64 (8.5)	27 (14.3)	26 (13.8)	7 (3.7)	4 (2.1)		
Hypertensive	23 (3.1)	8 (4.2)	6 (3.2)	8 (4.3)	1 (0.5)		
Previous medications, n (%)							
Aspirin	282 (37.4)	82 (43.4)	78 (41.3)	67 (35.6)	55 (29.3)	0.02	< 0.01
P2Y12 inhibitors	124 (16.4)	35 (18.5)	33 (17.5)	28 (14.9)	28 (14.9)	0.71	0.27
Anticoagulant	162 (21.5)	56 (29.6)	61 (32.3)	54 (28.7)	42 (22.3)	0.18	0.08
ACE inhibitors	285 (37.8)	74 (39.2)	81 (42.9)	71 (37.8)	59 (31.4)	0.14	0.07
Sacubitril/valsartan	18 (2.5) (n = 714)	3 (1.7) (n = 181)	5 (2.8) (n = 181)	5 (2.8) (n = 178)	5 (2.9) (n = 174)	0.86	0.48
Statins	279 (37.0)	87 (46.0)	80 (42.3)	64 (34.0)	48 (25.5)	< 0.01	< 0.01
Betablockers	310 (41.1)	93 (49.2)	75 (39.7)	76 (40.4)	66 (35.1)	0.04	< 0.01
Loop diuretics	369 (48.9)	109 (57.7)	107 (56.6)	80 (42.6)	73 (38.8)	< 0.01	< 0.01
Aldosterone antagonist	107 (14.2)	26 (13.8)	33 (17.5)	21 (11.2)	27 (14.4)	0.38	0.69
Amiodarone	130 (17.7) (n = 736)	42 (23.2) (n = 181)	33 (17.7) (n = 186)	24 (13.1) (n = 183)	31 (16.7) (n = 186)	0.09	0.06
SCAI Stage, n (%)							
B	62 (8.2) (n = 753)	14 (7.4)	13 (6.9) (n = 188)	13 (6.9)	22 (11.7)	0.29	0.15
C	257 (34.1) (n = 753)	61 (32.3)	64 (34.0) (n = 188)	67 (35.6)	65 (34.6)		0.58
D	328 (43.6) (n = 753)	91 (48.1)	90 (47.9) (n = 188)	76 (40.4)	71 (37.8)		0.02
E	106 (14.1) (n = 753)	23 (12.2)	21 (11.2) (n = 188)	32 (17.0)	30 (16.0)		0.13
CS triggers, n (%)							
Ischemic	278 (36.9)	67 (35.4)	61 (32.3)	77 (41.0)	73 (38.8)	0.32	0.23

Table 1 (continued)

	Overall population (n = 754)	Quartile 1 (< 11.0) (n = 189)	Quartile 2 (11.0–12.6) (n = 189)	Quartile 3 (12.6–14.0) (n = 188)	Quartile 4 (14.1–21.7) (n = 188)	p value	P_{trend}
Supraventricular tachycardia	102 (13.5)	18 (9.5)	20 (10.6)	29 (15.4)	35 (18.6)	0.03	< 0.01
Infectious disease	90 (11.9)	37 (19.6)	23 (12.2)	19 (10.1)	11 (5.9)	< 0.01	< 0.01
Ventricular arrhythmia	95 (12.6)	23 (12.2)	17 (9.0)	28 (14.9)	27 (14.4)	0.30	0.25
Iatrogenesis	44 (5.8)	9 (4.8)	10 (5.3)	17 (9.0)	8 (4.3)	0.18	0.77
Non-observance	26 (3.4)	5 (2.6)	7 (3.7)	7 (3.7)	7 (3.7)	0.92	0.58
Mechanical complications	22 (2.9)	3 (1.6)	8 (4.2)	7 (3.7)	4 (2.1)	0.36	0.84
Conduction disorder	17 (2.3)	6 (3.2)	6 (3.2)	2 (1.1)	3 (1.6)	0.39	0.16

ACE angiotensin-converting enzyme, *BB* betablockers, *COPD* = chronic obstructive pulmonary disease, *ICD* implantable cardioverter-defibrillator, *NYHA* New York Heart Association, *PCI* percutaneous coronary intervention, *SD* standard deviation

commonly had a history of cardiomyopathy (increasing from 46.3% to 63.0% between Q4 and Q1, p < 0.01, Ptrend < 0.01), particularly of ischemic and valvular origin, which was associated with a higher rate of previous implantable cardioverter-defibrillator (ICD) (p = 0.02, Ptrend = 0.04)) and more frequent use of beta-blockers and loop diuretics (both with p < 0.01 and Ptrend < 0.01). Based on our adapted classification, 62 patients (8.2%) were categorized as SCAI shock stage B, 257 (34.1%) as SCAI stage C, 328 (43.6%) as SCAI stage D, and 106 (14.1%) as SCAI stage E, with a significant trend towards an increase in the proportion of stage D from Q4 to Q1 (Ptrend = 0.02). AMI was the primary cause of CS in 36.9% of cases and was evenly distributed across quartiles, whereas infectious triggers were more frequent among Q1 patients (decreasing from 19.6% in Q1 to 5.9% in Q4, p < 0.01, Ptrend < 0.01).

CS presentation and prognostic markers in the four quartiles of Hemoglobin

As delineated in Table 2, the four quartiles exhibited discernible variations with respect to certain prognostic indicators. Notably, systolic, diastolic, and mean blood pressures were all significantly lower in Q1 (p < 0.01), with a clear trend observed across quartiles (Ptrend < 0.01) for all three measures. They also presented with signs of right heart failure in 57.2% of cases (compared to 43.3% in Q4, p = 0.03, Ptrend < 0.01). From a biological standpoint, a lower Hb level was associated with higher levels of creatinine and natriuretic peptides (both NT-proBNP and BNP), as well as a lower prothrombin time, all demonstrating a highly significant trend (Ptrend < 0.01). No significant difference was found for skin mottling, signs of left heart failure, and medical history of initial cardiac arrest.

In-hospital management according to the four quartiles of hemoglobin

Data on in-hospital management are presented in Table 3. Notably, patients in the lowest Hb quartile (Q1) were administered norepinephrine significantly more frequently than those in Q4 (63.0% vs. 47.6%, p = 0.02, Ptrend < 0.01). Additionally, patients in Q1 also required RRT significantly more often (26.5% in Q1 vs. 11.2% in Q4, p < 0.01, Ptrend < 0.01) and had a markedly higher need for RBC transfusion support (31.2% in Q1 vs. 11.2% in Q4, p < 0.01, Ptrend < 0.01). Lastly, a decreasing trend was observed in the use of microaxial flow pumps across quartiles with lower Hb levels (Ptrend < 0.01).

CS evolution according to quartiles of hemoglobin

First, whether at 1 month (Ptrend = 0.035) or 1 year (Ptrend < 0.01), a strong significant trend towards increased all-cause mortality was observed across Hb quartiles, suggesting a gradual correlation between quartiles of Hb level and all-cause mortality (Fig. 2). Specifically, compared with the Q4 group (taken as reference), Q1 patients demonstrated a 1.64-fold higher mortality rate at one month (95% CI: 1.09–2.47, p = 0.02), which amplified at one year, with a 2.53-fold increase in events (95% CI: 1.84–3.49, p < 0.01). Patients from the Q2 group also showed increased mortality at 1 month (HR 1.65 [95% CI 1.10–2.48], p = 0.02), which was also further confirmed and amplified at 1 year (HR 2.01, 95% CI 1.44–2.79), p < 0.01). In a multivariate Cox regression model (adjusted for baseline characteristics, left ventricular ejection fraction [LVEF], arterial blood lactate levels, CS triggers, aMCS, acute renal replacement therapy,

Table 2 Clinical, echocardiographic, and laboratory parameters according to hemoglobin level on the first day of management

	Overall population (n = 754)*	Quartile 1 (< 11.0) (n = 189)*	Quartile 2 (11.0 – 12.6) (n = 189)*	Quartile 3 (12.6 – 14.0) (n = 188)*	Quartile 4 (14.1 – 21.7) (n = 188)*	p value	P_{trend}
Clinical presentation at admission							
Heart rate, mean ± SD, bpm	95.7 ± 29.7	92.0 ± 27.1	93.6 ± 27.7	94.4 ± 30.8	102.9 ± 32.1	< 0.01	< 0.01
SBP, mean ± SD, mmHg	100.9 ± 24.8	95.5 ± 21.5	100.9 ± 23.3	99.3 ± 24.5	108.0 ± 28.0	< 0.01	< 0.01
DBP, mean ± SD, mmHg	63.0 ± 17.3	57.2 ± 14.4	62.4 ± 16.3	62.6 ± 17.9	69.7 ± 18.5	< 0.01	< 0.01
MBP, mean ± SD, mmHg	74.7 ± 18.3	69.5 ± 14.9	73.8 ± 17.5	74.7 ± 17.9	80.9 ± 20.6	< 0.01	< 0.01
Sinus rhythm, n (%)	387 (51.5)	90 (47.6)	97 (51.6)	99 (52.7)	101 (54.3)	0.61	0.20
Skin mottling, n (%)	251 (38.7)	59 (36.6)	63 (38.0)	69 (42.6)	60 (37.5)	0.69	0.67
Left heart failure, n (%)	544 (72.2)	137 (72.5)	139 (73.5)	134 (71.3)	134 (71.7)	0.96	0.74
Right heart failure, n (%)	367 (48.9)	107 (57.2)	95 (50.3)	84 (44.7)	81 (43.3)	0.03	< 0.01
Cardiac arrest, n (%)	76 (10.1)	19 (10.1)	16 (8.5)	22 (11.7)	19 (10.1)	0.78	0.73
Bleeding, n (%)	94 (13.1)	25 (13.7)	20 (11.4)	28 (15.6)	21 (11.6)	0.60	0.84
Blood tests at admission, median (IQR)							
Sodium, mmol/L	135.0 (132.0–139.0)	135.0 (131.0–138.0)	135.0 (131.0–138.0)	135.0 (132.0–139.0)	137.0 (133.0–140.0)	< 0.01	< 0.01
Potassium, mmol/L	4.0 (4.0–5.0)	4.0 (4.0–5.0)	4.0 (3.8–5.0)	4.0 (4.0–5.0)	4.0 (4.0–5.0)	0.74	0.48
Creatinin, µmol/L	133.0 (96.0–190.0)	152.0 (109.0–212.0)	139.0 (97.0–206.0)	122.5 (92.0–182.8)	118.0 (93.0–146.0)	< 0.01	< 0.01
Bilirubin, mg/L	16.0 (9.0–29.0)	13.8 (8.0–24.3)	16.1 (9.5–28.5)	16.0 (10.0–29.0)	17.0 (11.0–35.3)	0.09	< 0.01
PaO2, mmHg	86.0 (70.0–99.0)	90.0 (72.5–130.5)	78.0 (64.0–101.0)	82.0 (67.0–111.0)	88.0 (67.3–115.5)	0.03	0.52
Arterial blood lactates, mmol/L	3.0 (2.0–4.7)	3.0 (1.9–5.0)	2.9 (1.9–4.0)	3.0 (2.0–4.8)	3.0 (2.0–5.0)	0.12	0.04
ASAT, UI/L	90.5 (39.0–300.3)	76.0 (33.0–224.5)	91.0 (38.0–272.0)	127.0 (40.0–367.0)	84.5 (44.8–346.5)	0.21	0.046
ALAT, UI/L	60.0 (27.0–182.8)	39.0 (20.5–186.5)	59.0 (23.0–163.5)	70.5 (27.0–237.0)	71.0 (40.0–159.5)	< 0.01	< 0.01
PT, %	59.0 (37.0–77.0)	52.0 (35.0–68.0)	60.5 (35.3–75.8)	59.0 (35.0–79.0)	65.0 (46.0–85.0)	< 0.01	< 0.01
Nt-proBNP, pg/mL	9,037 (4,051.5–23,256.0)	16,109.0 (6,924.8–35,000.0)	13,138.0 (5,007.0–31,836.8)	6,410.0 (3,509.5–14,150.5)	6,595.5 (2,454.5–12,272.3)	< 0.01	< 0.01
BNP, pg/mL	1,147 (476.5–2,767.5)	1,504.5 (473.8–2,838.5)	1,540.0 (794.0–3,912.0)	847.0 (325.8–2,296.5)	963.0 (465.8–1,939.3)	< 0.01	< 0.01
ScvO2, %	71.0 (54.5–95.5)	87.5 (61.8–96.0)	65.0 (54.0–94.5)	64.0 (52.0–95.5)	67.0 (51.0–87.0)	0.20	0.54
Baseline echocardiography							
LVEF, median (IQR), %	24.0 (15.0–35.0)	30.0 (20.0–40.0)	23.0 (15.0–35.0)	25.0 (16.5–35.0)	20.0 (15.0–30.0)	< 0.01	< 0.01
TAPSE, median (IQR), mm	13.0 (10.0–16.5)	12.0 (9.5–16.5)	12.5 (9.0–17.0)	14.0 (10.0–17.0)	12.0 (10.0–16.0)	0.73	0.95
Severe mitral regurgitation, n (%)	105 (14.6)	31 (17.5)	29 (16.0)	25 (13.7)	20 (11.2)	0.35	0.07
Severe aortic stenosis, n (%)	34 (4.6)	10 (5.4)	12 (6.4)	6 (3.2)	6 (3.2)	0.35	0.15

ALAT alanine aminotransferase, *ASAT* aspartate aminotransferase, *BNP* Brain natriuretic peptide, *DBP* diastolic blood pressure, *IQR* interquartile range, *LVEF* left ventricular ejection fraction, *MBP* mean blood pressure, *Nt-proBNP* N-terminal-pro hormone BNP, *PaO2* arterial oxygen pressure, *PT* prothrombin time, *SBP* systolic blood pressure, *SD* standard deviation, *TAPSE* tricuspid annular plane systolic excursion

* Total counts may vary due to missing data

Table 3 In-hospital management according to hemoglobin level on the first day of management

	Overall population (n = 754)	Quartile 1 (< 11.0) (n = 189)	Quartile 2 (11.0–12.6) (n = 189)	Quartile 3 (12.6–14.0) (n = 188)	Quartile 4 (14.1–21.7) (n = 188)	p value	P_{trend}
Medications used, n (%)							
Dobutamine	617 (82.0) (n = 752)	145 (76.7)	159 (84.6) (n = 188)	165 (87.8)	148 (79.1) (n = 187)	0.02	0.40
Norepinephrine	407 (54.1) (n = 752)	119 (63.0)	103 (54.8) (n = 188)	96 (51.1)	89 (47.6) (n = 187)	0.02	< 0.01
Epinephrine	94 (12.5) (n = 752)	28 (14.8)	20 (10.6) (n = 188)	19 (10.1)	27 (14.4) (n = 187)	0.37	0.87
Levosimendan	57 (7.6) (n = 752)	14 (7.4)	13 (6.9) (n = 188)	15 (8.0)	15 (8.0) (n = 187)	0.97	0.74
Loop diuretics	460 (67.3) (n = 684)	119 (70.0) (n = 170)	123 (72.4) (n = 170)	99 (59.3) (n = 167)	119 (67.2) (n = 177)	0.06	0.19
Respiratory support, n (%)							
Non-invasive	199 (26.5) (n = 752)	43 (22.8)	52 (27.7) (n = 188)	47 (25.0)	57 (30.5) (n = 187)	0.36	0.15
Invasive	287 (38.2) (n = 752)	82 (43.4)	61 (32.4) (n = 188)	74 (39.4)	70 (37.4) (n = 187)	0.18	0.47
Acute MCS, n (%)							
IABP	48 (6.4)	8 (4.2)	11 (5.8)	18 (9.6)	11 (5.9)	0.19	0.28
Microaxial flow pump	25 (3.3)	2 (1.1)	5 (2.6)	8 (4.3)	10 (5.3)	0.10	0.01
ECLS	83 (11.0)	22 (11.6)	16 (8.5)	19 (10.1)	26 (13.8)	0.39	0.42
Renal replacement therapy, n (%)	120 (15.9) (n = 753)	50 (26.5)	26 (13.8)	23 (12.2)	21 (11.2) (n = 187)	< 0.01	< 0.01
Transfusion, n (%)	127 (16.9) (n = 751)	59 (31.2)	25 (13.4) (n = 187)	22 (11.7)	21 (11.2) (n = 187)	< 0.01	< 0.01

ECLS extracorporeal life support, *IABP* intra-aortic balloon pump, *MCS* mechanical circulatory support, *PCI* percutaneous coronary intervention

invasive respiratory support, and arterial oxygen pressure), low hemoglobin levels emerged as one of the few significant cofactors associated with all-cause mortality, both at 1 month (aHR 1.76 [95% CI 1.02–3.04], p = 0.04 and 1.72 [95% CI 1.03–2.87], p = 0.04 for Q1 and Q2, respectively, compared with Q4) and at 1 year (aHR 2.13 [95% CI 1.40–3.24], p < 0.01 and 1.83 [95% CI 1.22–2.73], p < 0.01 for Q1 and Q2, respectively, compared with Q4) (Table 4). The sensitivity analysis performed through multivariate logistic regression yielded similar results, with significantly increased 30-day mortality for Q1 (aOR 1.11 [1.01–1.23], p = 0.04) and Q2 (aOR 1.12 [1.02–1.25], p = 0.02) as well as 1-year mortality for Q1 (aOR 1.24 [1.10–1.39], p < 0.01) and Q2 (aOR 1.18 [1.06–1.32], p < 0.01) (Supplementary Table 1).

Restricted cubic spline curves

Monotonic relationships between Hb level and all-cause mortality were confirmed by spline analysis results, with P-overall at 0.04 and < 0.01 for 1-month and 1-year mortality (Fig. 3). The optimal cut-off for Hb's impact on 1-month mortality was 12.6 g/dL and 12.7 g/dL for 1-year mortality. Besides, the p-value for non-linearity was higher than 0.05, suggesting a possible linear association between Hb and mortality.

Subgroups analysis

First, we observed that the relationship between Hb levels and mortality in the overall population does not seem to apply specifically to women, either at 1 month (Ptrend = 0.9) or 1 year (Ptrend = 0.09), with no quartile showing a significant association. In contrast, this relationship is similarly expressed in men, with a 2.02-fold higher mortality rate at 1 month (95% CI 1.25–3.26, p < 0.01) and a 2.84-fold increase in events at 1 year (95% CI 1.94–4.14, p < 0.01) (Supplementary Fig. 2). Moreover, no significant trend was found between Hb levels and mortality for patients with CKD (Ptrend = 0.53 at one month and 0.43 at one year), with no quartile reaching statistical significance. However, the link between anemia and mortality was again highlighted in non-CKD patients, with higher mortality observed in the Q1 group at both 1 month (HR 1.69 [95% CI 1.06–2.70], p = 0.03) and 1 year (HR 2.47 [95% CI 1.72–3.57], p < 0.01) (Supplementary Fig. 3). Besides, a lower Hb level was still associated with increased mortality for AMI-CS patients at 1 year (P trend < 0.01, HR 2.17 [1.32–3.56], p < 0.01), but not at 1 month (P trend = 0.57, with no quartile being significant). In contrast, a strong negative impact of anemia on mortality was observed for NICS patients, with a 1-month HR ranging from 2.10 to 2.86 for the first three quartiles (P trend < 0.01), which persisted at 1 year for Q1 (HR 2.59 [1.72–3.91], p < 0.01) and Q2 (HR 2.65 [1.76–3.99], p < 0.01) (Supplementary Fig. 4). Eventually, the detrimental effect of low hemoglobin levels was also observed in patients aged < 67 years, at both 1-month (HR for Q1: 1.90 [1.05–3.46], p = 0.04, Ptrend = 0.03) and 1-year (HR for Q1: 2.94 [1.85–4.66], p < 0.01,

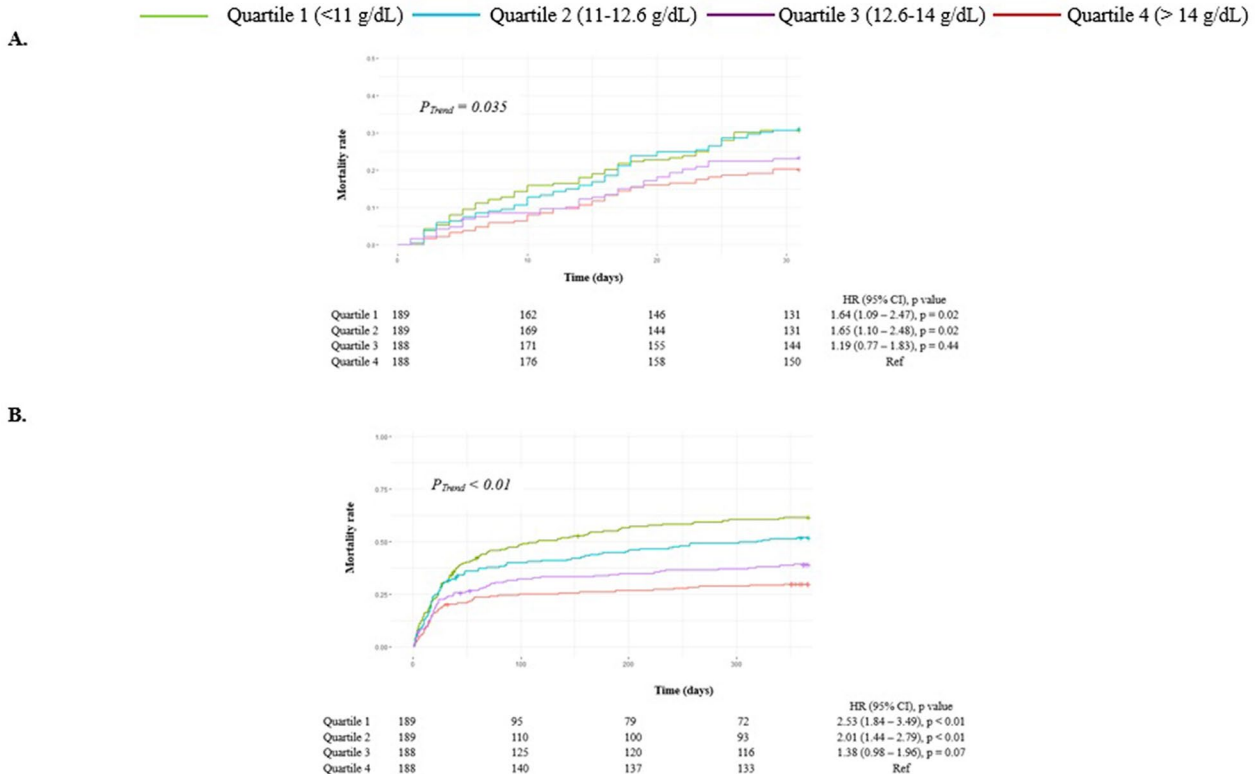


Fig. 2 Short- and long-term mortality outcomes after CS according to baseline hemoglobin level. **A** represents 1-month overall mortality. **B** focuses on 1-year mortality. The cumulative incidences of 1-year and 1-month mortality were estimated with the use of the Kaplan–Meier method; hazard ratios and 95% confidence intervals were estimated with the use of Cox regression models. Patients were categorized into four quartiles based on their hemoglobin level at admission: Quartile 1 group with a Hb < 11.0 g/dL, Quartile 2 group with Hb levels ranging from 11.0 to 12.6 g/dL, Quartile group with Hb levels ranging from > 12.6 to 14.0 g/dL, and Quartile with Hb > 14.0 g/dL. *CS* cardiogenic shock, *HR* hazard ratio

Ptrend < 0.01). In contrast, for patients aged ≥ 67 years, the negative effect of anemia was only observed at 1 year (Supplementary Fig. 5).

Discussion

In this study, we demonstrate that baseline hemoglobin level provides valuable prognostic insights for patients admitted with CS. While very little is known about the consequences and management of anemia in CS patients, we report that: (1) anemia is a common condition, affecting nearly half of ICU/ICCU-admitted CS patients at admission; (2) there is a strong, monotonic, independent, and gradual relationship between low hemoglobin levels and mortality, with higher hemoglobin levels being associated with a better prognosis; (3) this negative impact appears to be heterogeneous across different subpopulations, as it was not confirmed in female patients, patients aged ≥ 67 years, or those with chronic kidney disease; and (4) low hemoglobin levels are strongly associated with higher mortality in non-ischemic CS.

Despite improved pharmacologic and device-based therapies, CS remains a complex challenge to the medical community, with mortality remaining unacceptably high [15]. Recent discussions on improving management focus, initially, on better phenotyping of CS patients, with a predominance of NICS, and addressing acute triggers in addition to optimizing factors contributing to hemodynamic instability [4, 15]. Although anemia is an extremely common phenomenon in daily practice [5, 6], with well-established deleterious consequences (reduced oxygen tissue delivery, impaired oxygen utilization, etc.), there are no specific recommendations for the management of anemia in CS patients, and no randomized trials have addressed this topic so far. Our study highlights that low Hb levels may play a pivotal role in identifying CS patients at higher risk of both short- and long-term deterioration and mortality, while also representing a potential therapeutic target. However, the optimal RBC transfusion strategy for this population remains to be determined. In the absence of specific data or tailored recommendations, CS patients are often managed using

Table 4 Description of all hazard ratios and 95% confidence intervals of all variables tested in multivariate analysis models for 1-month and 1-year all-cause mortality

	1-month		1-year	
	aHR (95% CI)	**p value**	**aHR (95% CI)**	**p value**
Hemoglobin				
< 11.0 g/dL (Q1)	1.76 (1.02–3.04)	0.04	2.13 (1.40–3.24)	< 0.01
11.0–12.6 g/dL (Q2)	1.72 (1.03–2.87)	0.04	1.83 (1.22–2.73)	< 0.01
12.6–14.0 g/dL (Q3)	1.03 (0.61–1.71)	0.92	1.19 (0.79–1.78)	0.40
≥ 14.0 g/dL (Q4)	Ref	–	Ref	–
Age (per year)	1.04 (1.03–1.06)	< 0.01	1.04 (1.02–1.05)	< 0.01
Male sex	1.05 (0.71–1.54)	0.81	1.05 (0.79–1.41)	0.73
BMI ≥ 25	1.01 (0.71–1.43)	0.95	0.90 (0.69–1.17)	0.41
Diabetes mellitus	0.71 (0.47–1.07)	0.10	0.89 (0.66–1.20)	0.46
Hypertension	0.95 (0.64–1.40)	0.79	0.84 (0.63–1.13)	0.25
Dyslipidemia	0.89 (0.60–1.31)	0.55	0.97 (0.73–1.30)	0.86
Current smoking	1.37 (0.89–2.11)	0.16	1.21 (0.87–1.68)	0.25
Peripheral artery disease	0.74 (0.42–1.31)	0.30	0.73 (0.49–1.10)	0.13
Chronic kidney disease	1.33 (0.88–2.00)	0.18	1.11 (0.82–1.51)	0.50
COPD	0.99 (0.52–1.90)	0.98	1.22 (0.77–1.94)	0.39
ICD	0.83 (0.50–1.38)	0.48	0.89 (0.62–1.28)	0.52
Active cancer	0.89 (0.45–1.78)	0.75	1.47 (0.93–2.33)	0.10
Stroke	0.96 (0.55–1.68)	0.89	1.04 (0.68–1.59)	0.84
Previous PCI	0.89 (0.58–1.37)	0.60	0.99 (0.72–1.35)	0.94
NYHA functional status ≥ 3	1.39 (0.96–1.99)	0.08	1.38 (1.04–1.81)	0.02
History of cardiac disease	0.91 (0.58–1.42)	0.67	1.30 (0.93–1.82)	0.12
LVEF ≤ 30%	2.20 (1.41–3.43)	< 0.01	1.50 (1.09–2.06)	0.01
Ischemic trigger	1.34 (0.90–2.00)	0.15	1.15 (0.85–1.55)	0.37
SVT trigger	1.13 (0.67–1.89)	0.65	1.03 (0.70–1.52)	0.88
Infectious trigger	1.51 (0.92–2.47)	0.10	1.31 (0.91–1.89)	0.14
VA trigger	1.22 (0.74–2.03)	0.43	1.23 (0.84–1.79)	0.29
Iatrogenesis trigger	0.96 (0.43–2.17)	0.92	0.95 (0.53–1.71)	0.86
Non-observance trigger	1.29 (0.60–2.75)	0.52	1.40 (0.80–2.45)	0.25
Mechanical complications trigger	1.77 (0.79–3.98)	0.16	1.17 (0.60–2.30)	0.64
Conduction disorder trigger	0.67 (0.20–2.31)	0.53	1.18 (0.54–2.54)	0.68
Sinus rhythm	0.84 (0.59–1.19)	0.32	0.86 (0.66–1.13)	0.28
Left heart failure	0.96 (0.65–1.43)	0.86	1.00 (0.75–1.34)	0.99
Right heart failure	1.03 (0.73–1.46)	0.87	0.90 (0.69–1.17)	0.44
Cardiac arrest	1.27 (0.71–2.26)	0.42	0.72 (0.44–1.17)	0.18
Lactates ≥ 4 mmol/L	1.33 (0.94–1.90)	0.11	1.29 (0.98–1.68)	0.07
Transfusion	0.79 (0.50–1.26)	0.33	1.06 (0.75–1.50)	0.73
Invasive respiratory support	1.33 (0.88–2.00)	0.17	1.21 (0.89–1.65)	0.22
Acute MCS	1.66 (1.04–2.64)	0.03	1.74 (1.21–2.50)	< 0.01
Renal replacement therapy	2.14 (1.42–3.22)	< 0.01	1.83 (1.34–2.50)	< 0.01
PaO2 (per 10 points)	1.01 (0.98–1.04)	0.67	1.01 (0.99–1.03)	0.46

aHR adjusted hazard ratio, *BMI* body mass index, *COPD* chronic obstructive pulmonary disease, *ICD* implantable cardioverter-defibrillator, *LVEF* left ventricular ejection fraction, *MCS* mechanical circulatory support, *NYHA* New York Heart Association, *PaO2* arterial oxygen pressure, *SVT* supraventricular tachycardia, *VA* ventricular arrhythmia

conventional RBC transfusion thresholds of 9 g/dL [7]. Recent observational data further complicate this issue, suggesting that a Hb threshold of Hb < 8 g/dL may be appropriate for RBC transfusions in most ICCU patients. Although these findings indicate no clear benefit of RBC transfusions at a nadir ≥ 10 g/dL, the authors could not

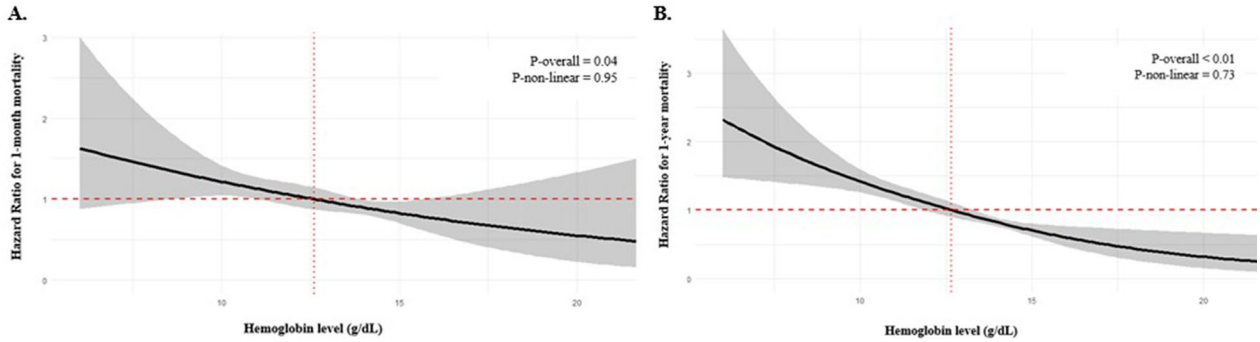


Fig. 3 Restricted cubic spline curves for the relationship between hemoglobin and all-cause mortality. **A** represents the restricted cubic spline curve for 1-month mortality. **B** represents the restricted cubic spline curve for 1-year mortality. The gray area represents the 95% confidence interval

exclude a potential benefit for patients with a nadir Hb of 8 to 9.9 g/dL [16]. This underscores the need for prospective studies to refine RBC transfusion strategies and determine the most effective thresholds in CS patients. Hence, future studies should focus on evaluating the comparison between "liberal" RBC transfusion strategies, allowing for higher RBC transfusion thresholds than traditionally used, and "restrictive" strategies, adhering to the usual thresholds. The impact of RBC transfusion strategies on outcomes in AMI has already been explored in the MINT study [8]. This trial demonstrated that a liberal transfusion goal (≥ 10 g/dL) was not superior to a restrictive strategy (Hb 7–8 g/dL) in terms of 1-month mortality, but remains inapplicable to CS patients where (1) unfavorable hemodynamic conditions drastically increase overall metabolic demand, relying, among other factors, on plasma Hb levels, and (2) most CS patients currently treated do not present with an acute ischemic trigger [17]. Similar findings were reported in the REALITY study, which demonstrated that a restrictive RBC transfusion strategy (transfusion for Hb ≤ 8 g/dL with a target Hb of 8–10 g/dL) was non-inferior to a more liberal strategy (transfusion for Hb ≤ 10 g/dL with a target Hb > 11 g/dL) regarding major adverse cardiovascular events at 30 days in anemic patients with AMI. Nevertheless, it is important to note that patients with CS were excluded from this study [18]. Furthermore, developing the optimal strategy for RBC transfusion remains challenging, as transfusion is further known to increase mortality in other conditions, such as AMI [19]. Its impact in the context of CS, however, remains underexplored due to the lack of prospective data. The exact nature of the relationship between anemia and mortality in CS remains to be clarified. Indeed, due to reduced oxygen tissue delivery, impaired oxygen utilization, and chronic tissue ischemia, anemia constitutes a direct detrimental factor, compromising functional reserve capacities and also hindering myocardial recovery [20]. Additionally, one could infer that, beyond its direct effect, anemia, with its numerous and varied etiologies (e.g., CKD, malnutrition, etc.), could be considered as an overall marker of comorbidity profiles that negatively affect the prognosis of CS patients. The significance of this second assertion seems tempered by the persistence of a statistically significant association between low Hb levels and mortality in our multivariate analysis (adjusted for baseline characteristics), as well as the absence of a link found in the specific subgroup of CKD patients. However, caution is warranted before drawing definitive conclusions, as these are observational data, and residual bias cannot be excluded. It could also be hypothesized that anemia, raising suspicion of a significant hemorrhagic risk (as incorporated, for example, in the PRECISE-DAPT Score [21]), partially limits the therapeutic options used in CS, whether in terms of antithrombotic treatments or the implementation of device-related therapies, such as microaxial flow pumps, where the associated hemorrhagic risk remains one of the main barriers and complications related to their use [22]. Thus, the exact nature of the underlying mechanisms of the detrimental effect of anemia in CS remains to be elucidated, particularly to understand why it does not seem to apply in certain subpopulations, such as female individuals in our study, even though anatomical, physiological, biological, genetic and pharmacological dimorphisms likely contribute to sex-specific responses in critically ill patients [23].

Even though several clinical scenarios can cause CS, the most frequently reported and extensively studied CS etiology is AMI [24], with substantial data enabling the development of various predictive factors and prognostic scores [25]. However, recent studies have indicated that only a minority of CS cases are explained by AMI infarction, whereas the majority were NICS cases, caused by decompensated heart failure [26]. In this field, our study is the first to shed light on the detrimental impact of low Hb levels in NICS patients, through a strong, gradual,

and independent relationship, with an effect that appears to be even more pronounced than in AMI-CS patients. Several explanations can be proposed to account for this observation. AMI-CS originates from myocardial damage due to a mismatch in oxygen supply and demand. Early revascularization can resolve this and still stands as the only evidence-based treatment for CS so far [1]. Additionally, if the patient is already in a state of ongoing CS, mechanical circulatory support devices might help support cardiac output until the damaged heart recovers, with recent encouraging results that remain to be further confirmed [22]. Conversely, non-ischemic CS typically manifests as acute HF (either as an acute decompensation in a chronic HF patient or as a de novo event) and can be caused by a variety of diseases. It can be hypothesized that, in the context of more chronic heart diseases, the mechanisms of cardiac output adaptation require maintaining an adequate Hb level to help compensate for the chronic impairment of a portion of cardiac output. However, we lack sufficient data to formally assert this, and our study should be considered hypothesis-generating. Further studies should investigate whether there might be a benefit to a higher RBC transfusion threshold in NICS. The same applies to other associated conditions, such as CKD, where there is likely an interaction between multiple pathophysiological phenomena. Indeed, while anemia is primarily attributed to decreased erythropoietin production, a recent RCT demonstrated that the systematic administration of erythropoietin after AMI did not yield beneficial effects on long-term outcomes [27], possibly indicating the overlap of several other unknown factors, warranting further investigation.

Limitations

The main limitation of our study is the absence of data related to iron deficiency (ID), particularly through ferritin or transferrin saturation levels. Indeed, ID has recently emerged as a major comorbidity in chronic and acute HF patients, as well as a strong and independent predictor of outcomes in this population, regardless of the presence of anemia [28]. Whether the negative impact of anemia in CS is ID-specific or not remains entirely unknown. The only observational study that has investigated this issue did not find any association between ID, irrespective of the presence or absence of anemia, and 1-month mortality or the frequency of RRT for CS patients [5]. Future studies could explore the potential benefit of iron supplementation, possibly combined with erythropoietin administration, either in conjunction with or independently of transfusion strategies. Besides, in the absence of universal recommendations, there is likely a degree of heterogeneity across the included centers, particularly regarding transfusion practices, which were conducted according to local protocols. Moreover, we do not have data on whether transfusion targets were met, preventing us from drawing definitive conclusions. Specifically, we lack detailed information on the clinical context surrounding transfusion decisions, and hemoglobin levels ≥ 11 g/dL were most likely not the result of intentional transfusion targets but rather reflect baseline levels in patients who were not transfused. As our observational data are subject to indication bias, and given the absence of prospective validation, we believe it would be inappropriate to infer a formal transfusion threshold from these findings.

Additionally, our study is based solely on the Hb level at the time of ICU/ICCU admission, which we consider a reliable reflection of the usual Hb level, unaltered by therapeutic interventions. However, it would be valuable to combine these data with information on the number of RBC transfusions performed and their effectiveness, potentially associated with iterative Hb measurements at discharge and during subsequent follow-up. Finally, we lacked key data on repeated measurements of oxygen saturation or the precise FiO_2 delivered, which would have allowed a more comprehensive assessment of oxygen delivery. This limitation may have affected our ability to fully address the interplay between hemoglobin concentration, oxygen saturation, and cardiac output in determining peripheral oxygen delivery.

Conclusion

Anemia is a very common condition frequently intertwined with cardiogenic shock, significantly worsening both short- and long-term mortality, particularly when baseline hemoglobin levels fall below 11 g/dL. Its effect appears heterogeneous and is influenced by the cardiogenic shock phenotype. Due to its frequency and detrimental impact, further randomized studies are highly needed to understand its underlying mechanisms and adapt the red blood cell transfusion strategy accordingly.

Abbreviations

ACE	Angiotensin-converting enzyme
aHR	Adjusted hazard ratio
ALAT	Alanine aminotransferase
aMCS	Acute mechanical circulatory support
AMI	Acute myocardial infarction
aOR	Adjusted odds ratios
ASAT	Aspartate aminotransferase
BB	Betablocker
BNP	Brain natriuretic peptide
CCTIRS	Comité consultatif pour le traitement de l'information en matière de recherche dans le domaine de la santé
CI	Confidence interval
CKD	Chronic kidney disease
CNIL	Commission nationale de l'informatique et des libertés
COPD	Chronic obstructive pulmonary disease
CS	Cardiogenic shock
DBP	Diastolic blood pressure

ECLS	Extracorporeal life support
HF	Heart Failure
HR	Hazard ratio
IABP	Intra-aortic balloon pump
ICU	Intensive care unit
ICCU	Intensive cardiac care unit
ICD	Implantable cardioverter-defibrillator
ID	Iron deficiency
IQR	Interquartile range
LVEF	Left ventricular ejection fraction
MBP	Mean blood pressure
MCS	Mechanical circulatory support
NICS	Non-ischemic cardiogenic shock
Nt-proBNP	N-terminal-pro hormone BNP
NYHA	New York Heart Association
PCI	Percutaneous coronary intervention
PSVtdi	Peak systolic velocity tissue Doppler Imaging
PT	Prothrombin time
RCS	Restricted cubic spline
RBC	Red blood cell
RCT	Randomized clinical trial
RRT	Renal replacement therapy
SBP	Systolic blood pressure
SD	Standard deviation
TAPSE	Tricuspid annular plane systolic excursion

Supplementary Information

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Supplementary material 1.

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None.

Author contributions
M. C., C. D.: made substantial contributions to the conception and design of the work, the acquisition, analysis, and interpretation of data, and drafted the work. F. R., H. M., P. G.: made substantial contributions to the analysis and interpretation of data and substantively revised the manuscript. B. L., E. P., E. B., F. V., M. E., O. M., G. L., N. L., E. G.: substantively revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was conducted per 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).

Consent for publication
All participants or their legal surrogates provided written informed consent for the collection, analysis, and publication of anonymized data. No identifying personal or clinical information of the participants is included in this manuscript.

Competing interests
The authors declare no competing interests.

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