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# **Cardiogenic shock in adults with congenital heart disease: Insights from the FRENSHOCK registry**

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\_Tweet: # 1st study on cardiogenic shock in ACHD patients.

# Rare but severe prognosis of cardiogenic shock in adults with congenital heart disease # SFC.

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#### **Keywords:**

Congenital heart disease Cardiogenic shock Prognosis.

#### **Abbreviations**

ACHD adults with congenital heart disease; CHD congenital heart disease; CI confidence interval; CS cardiogenic shock; non-ACHD adults without congenital heart disease ;VAD ventricular assist device.

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## **a b s t r a c t**

#### **Background:**

Data on cardiogenic shock in adults with congenital heart disease (ACHD) are scarce. Aim: We sought to describe cardiogenic shock in ACHD patients in a nationwide cardiogenic shock registry.

#### **Methods:**

From the multicentric FRENSHOCK registry (772 patients with cardiogenic shock from 49 French centres between April and October 2016), ACHD patients were compared with adults without congenital heart disease (non-ACHD). The primary outcome was defined by all-cause mortality, chronic ventricular assist device or heart transplantation at 1 year.

#### **Results:**

Out of the 772 patients, seven (0.9%) were ACHD, who were younger (median age: 56 vs. 67 years), had fewer cardiovascular risk factors, such as hypertension (14.3% vs. 47.5%) and diabetes (14.3% vs. 28.3%), and no previous ischaemic cardiopathy (0 vs. 61.5%). Right heart catheterization (57.1% vs. 15.4%), pacemakers (28.6% vs. 4.6%) and implantable cardioverter-defibrillators (28.6% vs. 4.8%) were indicated more frequently in the management of ACHD patients compared with non-ACHD patients, whereas temporary mechanical circulatory support (0 vs. 18.7%) and invasive mechanical ventilation (14.3% vs. 38.1%) were less likely to be used in ACHD patients. At 1 year, the primary outcome occurred in 85.7% (95% confidence interval: 42.1–99.6) ACHD patients and 52.3% (95% confidence interval: 48.7–55.9) non-ACHD patients. Although 1-year mortality was not significantly different between ACHD patients (42.9%) and non-ACHD patients (45.4%), ventricular assist devices and heart transplantation tended to be more frequent in the ACHD group.

### **Conclusions:**

Cardiogenic shock in ACHD patients is rare, accounting for only 0.9% of an unselected cardio-genic shock population. Despite being younger and having fewer co-morbidities, the prognosis of ACHD patients with cardiogenic shock remains severe, and is similar to that of other patients.

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## **2-Background**

Advances in the medical and surgical care of children with congenital heart disease (CHD) have enabled more than 90% of them to survive to adulthood, and adults account now for over two thirds of the contemporary CHD population in Western countries [1]. Although outcomes are improved, surgery does not cure CHD, and late-onset complications, such as heart failure, are increasing. Consequently, the medical complexity of surviving patients with CHD has increased substantially over the last 2 decades. Heart failure is the most common complication in adults with CHD (ACHD), with a life prevalence of at least 30% in most patients with complex underlying diagnoses, and heart failure has become the leading cause of premature death, accounting for one third of all deaths [2–4].

ACHD patients with heart failure frequently present with more advanced disease than adults without CHD (non-ACHD) [5], but they seem less likely to be treated with advanced cardiac therapies, such as mechanical circulatory support or heart transplantation, than non-ACHD patients [6,7]. Management of heart failure is very challenging in these patients because of inherent structural variations, with their associated physiological consequences [8,9]. Recent consensus from the European Society of Cardiology and the American Heart Association

have been published to help clinicians with the management of chronic heart failure in ACHD patients [10,11]. However, few data concern the management of acute heart failure, and even fewer pertain to cardiogenic shock (CS). CS is defined as a state of low cardiac output resulting in end-organ hypoperfusion, signalling primary cardiac failure, and can result in multiorgan dysfunction and death [12].

We aimed to describe CS in ACHD patients from the largest European nationwide multicentre prospective registry on CS, and to compare characteristics, management and outcomes of CS between ACHD and non-ACHD patients.

## **3-Methods**

### **3.1. Overall patient population.**

This study was a sub-study of the prospective multicentre observational FRENSHOCK registry conducted in metropolitan France between April and October 2016, and involving 49 critical care units (ClinicalTrials.gov identifier: NCT02703038). The main objective was to describe the characteristics, management and outcome of patients with CS [13]. Briefly, all adult patients (aged  $\geq 18$  years) with CS were prospectively enrolled when they met at least one criterion of each of the following three components: (1) haemodynamic criteria, including low systolic blood pressure ( $< 90$  mmHg) and/or the need for maintenance with vasopressors/inotropes and/or a low cardiac index ( $< 2.2$  L/min/m<sup>2</sup>); (2) left and/or right heart pressure elevation (based on clinical signs, chest X-ray, blood tests, echocardiography or invasive haemodynamic measurements); and (3) clinical and/or biological signs of organ hypoperfusion. Patients admitted after cardiopulmonary resuscitation were included if they fulfilled previously defined CS criteria. Patients could be included regardless of CS aetiology or whether the CS was primary or secondary. Exclusion criteria were refusal or inability to consent and a diagnosis of CS refuted in favour of alternative diagnoses (septic shock, refractory cardiac arrest, postcardiotomy CS).

### **3.2. Data collection**

Baseline characteristics, including demographics (age, sex, body mass index and employment status), risk factors, medical history and previous medication were collected in the FRENSHOCK registry. Course before the critical care unit, and clinical, biological and echocardiographic data within the first 24 hours after intensive care unit admission were recorded. CS triggers, cardiac procedures, organ replacement therapies and in-hospital complications were also recorded. Outcomes at 30-day and 1-year follow-up included treatments, all-cause mortality and chronic ventricular assist device (VAD) or heart transplantation [14]

### **.3.3. ACHD population**

CHD was reported by investigators in the electronic reporting form, allowing for easy identification of the ACHD population. CHD complexity was classified as mild, moderate or severe according to the anatomical classification from the European Society of Cardiology guidelines for the management of ACHD [10]. All ACHD patients were identified in the database, and specific information concerning their medical history, especially surgeries or interventional procedures, were collected a posteriori through direct contact with the investigator site.

### **3.4. Ethics**

Written consent was obtained for all the patients. The data recorded and their handling and storage were reviewed and approved by the CCTIRS (French Health Research Data Processing Advisory Committee) (No. 15.897) and the CNIL (French Data Protection Agency) (No. DR-2016-109).

### **3.5. Statistical analysis**

Continuous data are reported as medians (interquartile ranges) and categorical data are reported in numbers and percentages, with 95% confidence intervals (CIs) provided whenever necessary. Survival curves were plotted using the Kaplan–Meier method to estimate 30-day and 1-year survival free from VAD or heart trans-plantation between ACHD and non-ACHD groups. All analyses were performed using Stata Standard Edition, version 17, 2021 (Stata-Corp LLC, Statistical Software, College Station, TX, USA).

## **4-Results**

### **4.1. Population**

Out of the 772 patients included in the FRENSHOCK registry, seven (0.9%) were ACHD patients (Table 1). ACHD patients were as follows: aortic bicuspid valve surgically repaired (n = 1); isolated atrial septal defect surgically closed (n = 1); atrial septal defect with abnormal pulmonary venous return surgically repaired (n = 1); unoperated congenitally corrected transposition of the great arteries (n = 2); transposition of the great arteries with atrial switch (Mustard) (n = 1); and tetralogy of Fallot repair (n = 2). Specific characteristics

of ACHD patients are described in Table 2. None of the CHDs was associated with a known genetic syndrome.

ACHD patients were younger (median age: 56 vs. 67 years), with fewer cardiovascular risk factors, such as hypertension (14.3% vs. 47.5%) and diabetes (14.3% vs. 28.3%), and no previous ischaemic cardiopathy (0 vs. 38.5%). Ischaemic trigger (28.6% vs. 36.4%) was less frequent in the ACHD group. History of pacemaker or implantable cardioverter-defibrillator was more common in ACHD patients (14.3% vs. 8.1% and 42.9% vs. 16.2%, respectively). Ventricular and supraventricular arrhythmia, as well as iatrogenicity and non-adherence to cardiac therapy were more frequent CS triggers in ACHD patients compared with non-ACHD patients (14.3% vs. 12.6%, 14.3% vs. 13.3%, 14.3 vs. 6.0% and 14.3 vs. 3.4%, respectively).

## **4.2. In-hospital management**

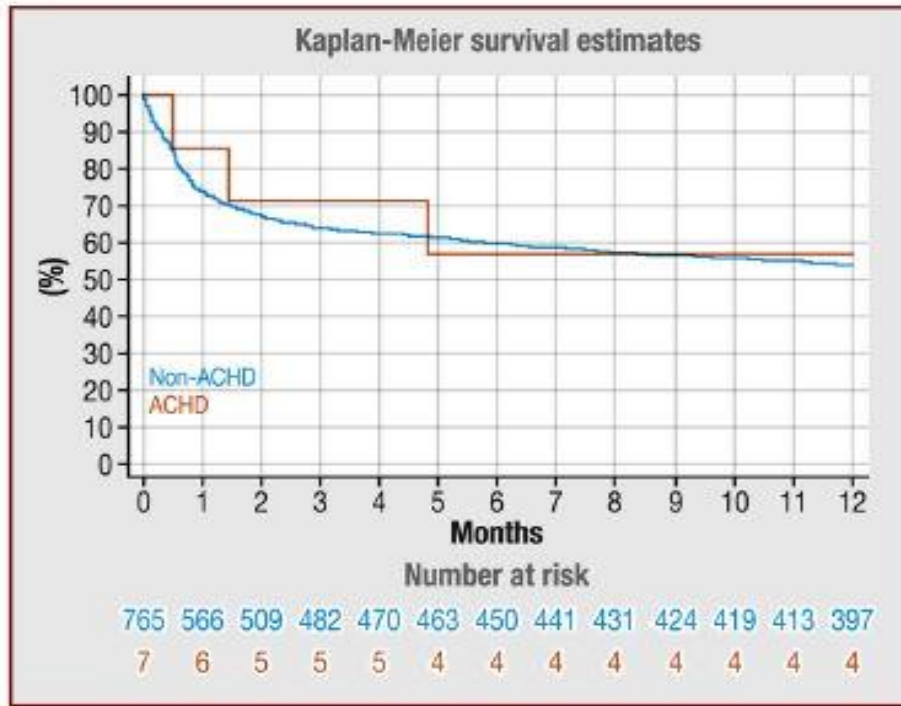
Table 3 compares in-hospital management between ACHD and non-ACHD patients. Right heart catheterization (57.1% vs. 15.4%), pacemaker implantation (28.6% vs. 4.6%) and implantable cardioverter-defibrillator implantation (28.6% vs. 4.8%) were performed more frequently in ACHD patients, whereas temporary mechanical circulatory support (0 vs. 18.7%) and invasive mechanical ventilation (14.3% vs. 38.1%) were more frequently indicated in the non-ACHD group.

## **4.3. Outcomes**

The 30-day mortality was 14.3% (95% CI: 0.4–57.9) in the ACHD group and 26.1% (95% CI: 23.1–29.4) in the non-ACHD group.

At 1-year follow-up, the primary outcome (death, heart transplantation or chronic VAD) had occurred in 85.7% (95% CI: 42.1–99.6) of ACHD patients and 52.3% (95% CI: 48.7–55.9) of non-ACHD patients. Fig. 1 depicts the corresponding Kaplan–Meier survival curves for ACHD and non-ACHD patients. Although 1-year mortality was not significantly different between the two groups (42.9%, 95% CI: 9.9–81.6 for ACHD patients; and 45.4%, 95% CI: 41.8–49.0 for non-ACHD patients), chronic VAD (14.3%, 95% CI: 0.4–57.9 vs. 5.4%, 95% CI: 3.9–7.2) and heart transplantation (28.6%, 95% CI: 3.7–71.0 vs. 5.2%, 95% CI: 3.8–7.0) tended to be more frequent in the ACHD group, although the difference was not statistically significant.<sup>5</sup>





**Fig. 1.** One-year survival free from chronic ventricular assist device or heart transplantation after cardiogenic shock in the FRENDSHOCK study according to the presence of congenital heart disease. ACHD: adult congenital heart disease.

## 5-Discussion

Based on a large nationwide prospective multicentre study on CS, we report, for the first time, data on CS in ACHD patients. The main results are as follows: (1) ACHD accounted for 0.9% of all CS in an unselected cohort from a broad spectrum of CS; (2) initial presentation is quite similar between ACHD and non-ACHD patients, despite younger age, fewer co-morbidities and more cardiac history; (3) in-hospital management is less invasive (less temporary mechanical circulatory support and mechanical ventilation), but needs more expert assessment with right heart catheterization; (4) early and long-term all-cause mortality rates are not different from those of non-ACHD patients (42.9% for ACVD patients vs. 45.4% for non-ACHD patients at 1 year); and (5) ACHD patients tend to benefit from more chronic VAD and heart transplantation.

**Table 1**

Baseline characteristics of patients with cardiogenic shock in the FRENSHOCK study, according to the presence of congenital heart disease.

	Total (n=772)	Non-ACHD group (n=765)	ACHD group (n=7)
Female sex	220(28.5)	218/765 (28.5)	2/7 (28.6)
Age (years); n	66.0 (58.0–77.0); 772	67.0 (58.0–77.0); 765	56.0 (46.0–62.0); 7
BMI (kg/m <sup>2</sup> ); n	24.6 (22.4–28.4); 744	24.8 (22.4–28.4); 738	21.3 (20.8–22.9); 6
Medical history			
Previous cardiopathy	429/771 (55.6)	426/764 (55.8)	3/7 (42.9)
Ischaemic cardiopathy	230/597 (38.5)	230/597 (38.5)	0/7 (0.0)
Pacemaker	63/771 (8.2)	62/764 (8.1)	1/7 (14.3)
ICD	127/771 (16.5)	124/764 (16.2)	3/7 (42.9)
CKD	164/771 (21.3)	163/764 (21.3)	1/7 (14.3)
Peripheral artery disease	91/771 (11.8)	91/764 (11.9)	0/7 (0.0)
Respiratory Insufficiency	8/771 (1.0)	8/764 (1.0)	0/7 (0.0)
COPD treated	50/771 (6.5)	49/764 (6.4)	1/7 (14.3)
Dialysis	11/771 (1.4)	11/764 (1.4)	0/7 (0.0)
Ischaemic stroke	62/771 (8.0)	62/764 (8.1)	0/0 (0.0)
Diabetes	217/770 (28.2)	216/763 (28.3)	1/7 (14.3)
Hypertension	364/771 (47.2)	363/764 (47.5)	1/7 (14.3)
Dyslipidaemia	277/771 (35.9)	276/764 (36.1)	1/7 (14.3)
Tobacco (current or past)	436/740 (58.9)	430/733 (58.7)	6/7 (85.7)
CS triggers			
Ischaemic	280/772 (36.3)	278/765 (36.3)	2/7 (28.6)
Ventricular arrhythmia	97/772 (12.6)	96/765 (12.6)	1/7 (14.3)
Supraventricular arrhythmia	103/772 (13.3)	102/765 (13.3)	1/7 (14.3)
Conductive disorder	18/772 (2.3)	18/765 (2.3)	0/7 (0.0)
Therapeutic non-adherence	27/772 (3.5)	26/765 (3.4)	1/7 (14.3)
Iatrogenic	47/772 (6.1)	46/765 (6.0)	1/7 (14.3)
Others	159/772 (20.6)	157/765 (20.5)	2/7 (28.6)
Baseline characteristics at inclusion			
Heart rate (bpm); n	92.0 (75.0–114.0); 769	92.5 (75.0–115.0); 762	92.0 (86.6–97.0); 7
Sinus rhythm	399/768 (52.0)	394/761 (51.8)	5/7 (71.4)
MAP (mmHg); n	73.0 (63.0–86.0); 767	73.0 (63.0–86.0); 760	91.0 (74.0–100.0); 7
Left heart failure signs	554/770 (72.0)	548/763 (71.8)	6/7 (85.7)
Right heart failure signs	377/768 (49.1)	373/761 (49.0)	4/7 (57.1)
LVEF (%); n	23.0 (15.0–35.0); 763	23.0 (15.0–35.0); 756	20.0 (15.0–40.0); 7
TAPSE (mm); n	13.0 (10.0–16.5); 260	13.0 (10.0–16.0); 257	13.0 (11.0–17.0); 3
S' tricuspid (cm/s); n	8.0 (6.0–11.0); 208	8.0 (6.0–11.0); 203	7.00 (7.0–9.0); 5
Natraemia (mmol/L); n	135.0 (132.0–139.0); 760	135.0 (132.0–139.0); 753	134.0 (128.0–137.0); 7
eGFR (mL/min/1.73 m <sup>2</sup> ); n	46.0 (28.0–67.0); 751	46.0 (28.0–67.0); 744	49.0 (31.0–60.0); 7
Arterial lactate (mmol/L); n	3.0 (2.0–4.73); 684	3.0 (2.0–4.7); 677	3.2 (2.0–4.8); 7
NT-proBNP (ng/L); n	9276 (4051–23,256); 224	9037 (4039–21,455); 221	24937 (5922–30,595); 3
BNP (pg/mL); n	1161.0 (476.0–2788.0); 265	982.0 (553.0–3524.0); 262	1153.0 (477.0–2788.0); 3
TGO (IU/L); n	90.0 (39.0–298.0); 549	88.50 (39.0–293.0); 542	189.0 (169.0–830.0); 7
TGP (IU/L); n	60.0 (27.0–183.0); 561	59.0 (27.0–181.0); 554	396.0 (112.0–775.0); 7
Treatments at baseline			
Aspirin	288/770 (37.4)	287/763 (37.6)	1/7 (14.3)
VKA	165/770 (21.4)	164/763 (21.5)	1/7 (14.3)
Non-VKA anticoagulant	56/770 (7.3)	55/763 (7.2)	1/7 (14.3)
ACE inhibitor/ARB	292/770 (37.9)	291/763 (38.1)	1/7 (14.3)
ARNi	18/728 (2.5)	18/721 (2.5)	0/7 (0)
Statin	286/770 (37.1)	286/763 (37.5)	0/7 (0)
Beta-blocker	316/770 (41.0)	313/763 (41.0)	3/7 (42.9)
Furosemide	376/770 (48.8)	371/763 (48.6)	5/7 (71.4)
MRA	108/770 (14.0)	106/763 (13.9)	2/7 (28.6)
Amiodarone	132/752 (17.6)	129/745 (17.3)	3/7 (42.9)
Other antiarrhythmic	31/747 (4.1)	30/740 (4.1)	1/7 (14.3)

Data are expressed as "number/number with data available (%)" or "median (interquartile range); number with data available". ACE: angiotensin-converting enzyme; ACHD: adult with congenital heart disease; ARB: angiotensin receptor blocker; ARNi: angiotensin receptor-neprilysin inhibitor; BMI: body mass index; BNP: brain natriuretic peptide; CKD: chronic kidney disease; COPD: chronic pulmonary obstructive disease; CS: cardiogenic shock; eGFR: estimated glomerular filtration rate; ICD: implantable cardioverter-defibrillator; LVEF: left ventricular ejection fraction; MAP: mean arterial pressure; MRA: mineralocorticoid receptor antagonist; NT-proBNP: N-terminal prohormone of brain natriuretic peptide; TAPSE: tricuspid annular plane systolic excursion; TGO: glutamic-oxaloacetic transaminase; TGP: glutamic pyruvic transaminase; VKA: vitamin K antagonist.

Data on CS in ACHD patients are extremely rare. In a single-centre cohort of Latino patients with acute heart failure (n = 21,042), 404 cases of CS were reported, including four (1%) ACHD patients, with an in-hospital mortality rate of 71.3% [14]. However, no clinical phenotypes, aetiologies or details about the management of this specific population were provided.

Whereas ACHD patients were younger and had fewer co-morbidities in our cohort, their prognosis seemed as poor as for the other patients. Cardiac history with frequent haemodynamic sequelae probably explains this result, justifying close monitoring of ACHD patients at risk of compromised haemodynamics, such as those with a single ventricle, systemic right ventricle or pulmonary arterial hypertension.

No temporary mechanical circulatory support was used during hospitalization for the ACHD patients in our study. Extracorporeal life support is commonly used as a mechanical circulatory support after cardiectomy [15,16], but was rarely reported for medical CS in ACHD patients. In a recent large cohort of 249 patients on extracorporeal life support, only two were ACHD, implanted for exacerbation of “chronic” heart failure [17]. The ACHD population is heterogeneous by definition, and often has complex underlying anatomy (such as abnormal situs, dextrocardia, azygos return, systemic right ventricle and malposition of the great arteries) and pathophysiology (Fontan circulation, residual shunt), which could pose a challenge to proposing temporary mechanical circulatory support, and may explain its underutilization.

Chronic VAD remains an option for ACHD patients, even if they represented < 0.1% (n = 126) of patients included in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) [7]. Nevertheless, the comparison of ACHD and non-ACHD patient outcomes in this database showed that ACHD patients were more likely to experience multisystemic organ failure, late-onset cardiac arrhythmia, infection and device malfunction compared with non-ACHD patients after VAD implantation [18].

Conversely, cardiac transplantation in ACHD has been well assessed [19]. Despite initial higher operative and post-operative risks in ACHD recipients, long-term prognosis seems similar, with 84.2% survival at 1 year and 69.7% at 5 years [20].

One-year all-cause mortality after CS is similar between ACHD and non-ACHD patients, affecting almost one in two patients, although ACHD patients are younger and with fewer co-morbid disorders. CS triggers were similar between the two groups. However, substrates of ventricular/supraventricular tachycardia triggers are mainly surgical scars in ACHD patients rather than myocardial ischaemia in non-ACHD patients [21]. Poor compliance and iatrogenic factors related to the medical treatment seemed more prevalent in ACHD patients, underlining the need for patient education about cardiac drugs and close monitoring of compliance. Referring to multidisciplinary expert centres should be the rule in the management of ACHD patients with CS, providing appropriate therapeutic interventions



through heart catheterization, electrophysiological procedures, temporary and chronic mechanical circulatory support and transplantation[22].

**Table 2**

Description of the adults with congenital heart disease (n = 7) included in the FREN-SHOCK registry.

Previous cardiac surgery	
One	6 (85.7)
Two or more	1 (14.3)
Socioprofessional background	
Disability or unemployment or work stoppage	3 (42.9)
Working	2 (28.6)
Retirement	2 (28.6)
Previous pulmonary hypertension	2 (28.6)
Previous endocarditis	1 (14.3)
Supraventricular tachycardia (atrial fibrillation or flutter)	4 (57.1)
VF or VT	2 (28.6)
Previous heart failure hospitalization	2 (28.6)

Data are expressed as number (%). VF: ventricular fibrillation; VT: ventricular tachycardia.

**Table 3**

In-hospital management and outcomes of patients with cardiogenic shock in the FREN-SHOCK registry, according to the presence of congenital heart disease.

	Total (n = 772)	Non-ACHD group (n = 765)	ACHD group (n = 7)
In-hospital management			
Medication			
Diuretics	633/768 (82.4) (79.5–85.1)	628/761 (82.5) (79.6–85.2)	5/7 (71.4) (29.0–96.3)
Vascular filling	321/767 (41.9) (38.3–45.4)	317/760 (41.7) (38.2–45.3)	4/7 (57.1) (18.4–90.1)
Dobutamine	632/768 (82.3) (79.4–84.9)	625/761 (82.1) (79.2–84.8)	7/7 (100) (59.0–1 <sup>a</sup> )
Norepinephrine	410/768 (53.4) (49.8–56)	407/761 (53.5) (49.9–57.1)	3/7 (42.9) (9.9–81.6)
Levosimendan	57/768 (7.4) (5.7–9.5)	55/761 (7.2) (5.5–9.3)	2/7 (28.6) (3.7–71.0)
Isoprenaline	32/768 (4.2) (2.9–5.9)	31/761 (4.1) (2.8–5.7)	1/7 (14.3) (0.4–57.9)
Amiodarone	278/752 (37.0) (33.5–40.5)	276/746 (37.0) (33.5–40.5)	2/7 (28.6) (3.7–71.0)
Other antiarrhythmic drugs	18/494 (3.6) (2.0–5.2)	18/487 (3.7) (2.0–5.4)	0/7 (0) (0–41.0 <sup>a</sup> )
In-hospital procedure			
Coronary angiography	399/772 (51.7) (44.7–51.9)	396/765 (51.8) (44.6–51.8)	3/7 (42.9) (18.4–90.1)
Right heart catheterization	121/768 (15.8) (13.3–18.5)	117/761 (15.4) (12.9–18.1)	4/7 (57.1) (18.4–90.1)
Endocavitary probe	30/768 (3.9) (2.7–5.6)	29/761 (3.8) (2.6–5.5)	1/7 (14.3) (0.4–57.9)
Pacemaker implantation	35/733 (4.8) (3.4–6.6)	33/726 (4.6) (3.2–6.3)	2/7 (28.6) (3.7–71.0)
ICD	37/733 (5.1) (3.6–6.9)	35/726 (4.8) (3.4–6.6)	2/7 (28.6) (3.7–71.0)
Atrial fibrillation/flutter radiofrequency ablation	17/733 (2.3) (1.4–3.7)	17/726 (2.3) (1.4–3.7)	0/7 (0) (0–0.41 <sup>a</sup> )
VF/VT radiofrequency ablation	16/733 (2.2) (1.6–3.5)	16/726 (2.2) (1.3–3.6)	0/7 (0) (0–41.0 <sup>a</sup> )
Organ support			
Non-invasive ventilation	176/768 (22.9) (20–26.1)	173/761 (22.7) (19.8–25.9)	3/7 (42.9) (9.9–81.6)
Invasive ventilation	291/768 (37.9) (34.5–41.4)	290/761 (38.1) (34.6–41.7)	1/7 (14.3) (0.4–57.9)
Mechanical circulatory support	143/770 (18.6) (15.9–21.5)	143/763 (18.7) (16.0–21.7)	0/7 (0) (0–41.0 <sup>a</sup> )
Renal replacement therapy	122/771 (15.8) (13.3–18.6)	122/764 (16.0) (13.4–18.8)	0/7 (0) (0–41.0 <sup>a</sup> )
In-hospital complications			
Bleeding	96/736 (13.0) (10.7–15.7)	95/729 (13.0) (10.7–15.7)	1/7 (14.3) (0.4–57.9)
Acute kidney injury	26/763 (3.4) (2.1–4.7)	25/756 (3.3) (2.0–4.6)	1/7 (14.3) (0.4–57.9)
Infection	255/738 (34.6) (31.1–38.1)	253/731 (34.6) (31.2–38.2)	2/7 (28.6) (3.7–71.0)
Stroke	36/739 (4.9) (3.4–6.7)	36/732 (4.9) (3.5–6.7)	0/7 (0) (0–41.0 <sup>a</sup> )
Characteristics at discharge			
LVEF (%) <sup>b</sup>	30 (25–45)	30 (25–45)	40 (30–50)
Death	217/770 (28.2) (25.0–31.5)	216/763 (28.3) (25.1–31.7)	1/7 (14.3) (0.4–57.9)
Heart transplantation	35/647 (5.4) (3.8–7.4)	33/641 (5.2) (3.6–7.2)	2/6 (33.3) (4.3–77.7)
VAD	11/635 (1.7) (0.9–3.1)	11/629 (1.7) (0.9–3.1)	0/6 (0) (0–45.9 <sup>a</sup> )
Medication at discharge			
Aspirin	322/547 (58.9) (54.8–63.0)	319/540 (59.1) (55.0–63.2)	3/7 (42.9) (6.2–79.6)
VKA	156/548 (28.5) (24.7–32.3)	155/541 (28.7) (24.9–32.5)	1/7 (14.3) (0.4–57.9)
Non-VKA anticoagulant	64/548 (11.7) (9.0–14.4)	63/541 (11.6) (8.9–14.3)	1/7 (14.3) (0.4–57.9)
ACE inhibitor/ARB	339/548 (61.9) (57.8–66.0)	337/541 (62.3) (58.2–66.4)	2/7 (28.6) (3.7–71.0)
ARNi	17/499 (3.4) (1.8–5.0)	17/492 (3.5) (1.9–5.1)	0/7 (0) (0–41.0 <sup>a</sup> )
Beta-blocker	306/548 (55.8) (51.6–60.0)	306/541 (56.6) (52.4–60.8)	0/7 (0) (0–41.0 <sup>a</sup> )
MRA	170/548 (31.0) (27.1–34.9)	169/541 (31.2) (27.3–35.1)	1/7 (14.3) (0.4–57.9)

Data are expressed as "number/number with data available (%) (95% confidence interval)". ACE: angiotensin-converting enzyme; ACHD: adult with congenital heart disease; ARB: angiotensin receptor blocker; ARNi: angiotensin receptor-neprilysin inhibitor; ICD: implantable cardioverter-defibrillator; LVEF: left ventricular ejection fraction; MRA: mineralocorticoid receptor antagonist; VAD: ventricular assist device; VF: ventricular fibrillation; VKA: vitamin K antagonist; VT: ventricular tachycardia.

<sup>a</sup> One-sided 97.5% confidence interval.

<sup>b</sup> Median of LVEF (25–75% CI).

## **5.1. Study limitations**

As an observational registry, the FRENHOCK registry faced the usual limitations. First, inclusions were probably neither exhaustive nor consecutive in all centres. Second, initial CS severity and mortality may have been underestimated, because patient consent was mandatory before inclusion as a result of administrative regulations; early death at admission may not have been included. Third, detailed aetiology of CS was not recorded in the electronic reporting form and, further, could not be precisely analysed (takotsubo cardiomyopathy, pulmonary embolism, acute decompensation of chronic heart failure, etc.); however, CS triggers were recorded. Fourth, an underestimation of ACHD declaration is possible, especially for mild CHD, such as aortic bicuspid valve or atrial septal defect, but is less probable for CHD with moderate or severe complexity. Fifth, despite a large national registry, the ACHD group was small ( $n = 7$ ), reflecting the low prevalence of ACHD in the general population, which precludes statistical comparison or propensity matching. However, because of the major increase in the number of adult patients with complex CHD, CS may be more prevalent in the future, justifying larger multicentre collection [23].

## **6. Conclusion**

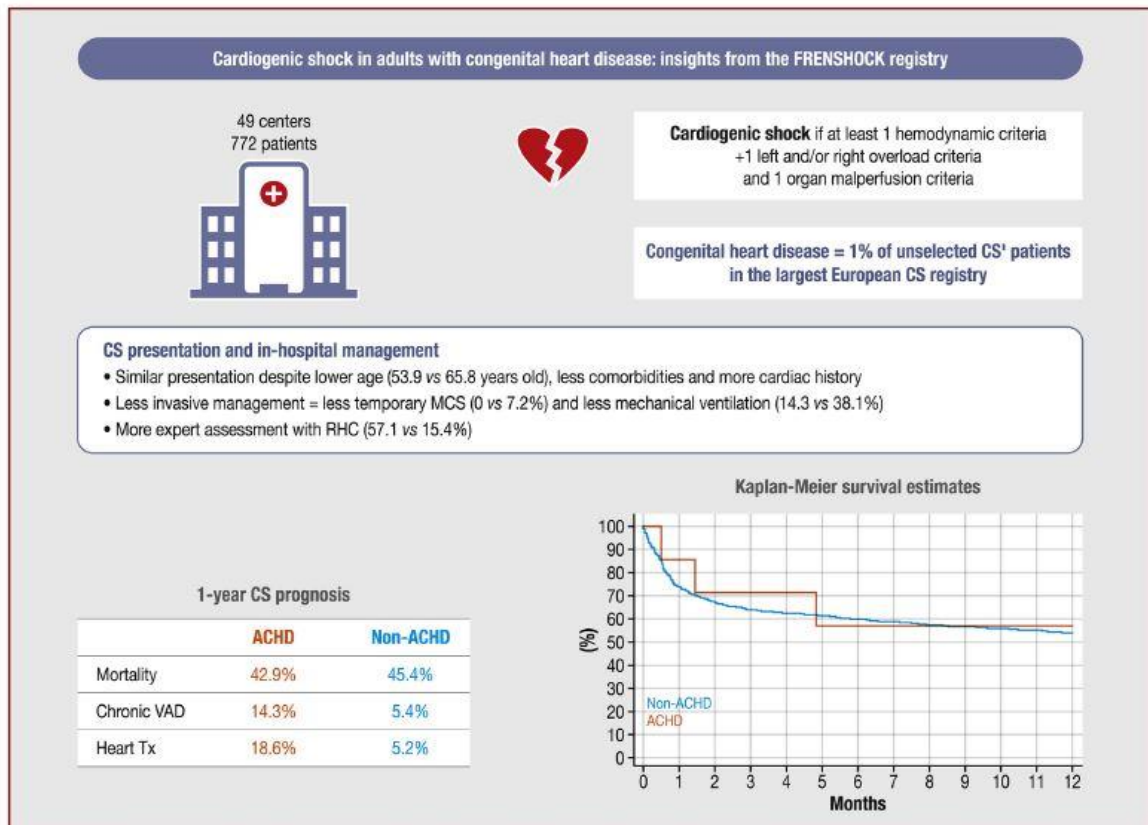
CS in ACHD is rare, accounting for only 0.9% of an unselected CS population. Despite a younger age and fewer co-morbidities, the prognosis of ACHD patients remains severe and similar to that of non-ACHD patients. ACHD present unique anatomical and physiological challenges that require multidisciplinary management in an expert centre to improve CS outcomes (Central Illustration). Central Illustration. Cardiogenic shock in adults with congenital heart disease: insights from the FRENHOCK registry. ACHD: adult congenital heart disease; CS: cardiogenic shock; MCS: mechanical circulatory support; RHC: right heart catheterization; VAD: ventricular assist device.

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### **Disclosure of interest**

The authors declare that they have no competing interest.



**Central Illustration.** Cardiogenic shock in adults with congenital heart disease: insights from the FRENDSHOCK registry. ACHD: adult congenital heart disease; CS: cardiogenic shock; MCS: mechanical circulatory support; RHC: right heart catheterization; VAD: ventricular assist device.

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