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Urgent balloon aortic valvuloplasty in patients with cardiogenic shock related to severe aortic stenosis: time matters

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KEYWORDS

- aortic stenosis
- balloon valvuloplasty
- cardiogenic shock
- TAVI

Abstract

Aims: The aim of the study was to assess the outcomes of balloon aortic valvuloplasty (BAV) as a rescue therapy in patients with cardiogenic shock (CS) related to severe aortic stenosis (AS).

Methods and results: Forty-four consecutive patients, n=31 with hypotensive CS (HCS) and n=13 with non-hypotensive CS (NHCS) due to acutely decompensated severe AS, from two centres were treated with urgent BAV. The composite primary endpoint was mortality or recurrent CS at one-year follow-up. These patients (77.3±8.1 years old; 75% male) had a mean EuroSCORE II of 41.6±13.7%. One-month mortality was 47%. Twelve patients (27%) had either a staged TAVR (n=10) or surgical aortic valve replacement (SAVR) (n=2) with a median delay of 79 days after BAV: n=6 (19%) in the HCS subgroup and n=6 (46%) in the NHCS population (p=0.06). At one year, the rate of composite all-cause death or recurrent CS was 75% and significantly higher in the HCS subgroup (83% vs. 53%; p=0.03). Overall one-year mortality was 70% (n=31) with a trend for a better prognosis in NHCS patients (54% vs. 77%; p=0.09). Univariate predictive factors of the primary endpoint included preoperative dose of dobutamine >5 microg/kg/min (100% vs. 57%; p=0.001) and delayed BAV >48 hrs (90% vs. 59%; p=0.01).

Conclusions: Despite the initial success of urgent BAV, morbidity and mortality of CS related to severe AS remain high and directly related to the time of the valvuloplasty. Performing BAV before or within 48 hours of starting inotropic agents appears to be key to survival.

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Abbreviations

AS	aortic stenosis
AVR	aortic valve replacement
BAV	balloon aortic valvuloplasty
BMI	body mass index
CS	cardiogenic shock
GFR	glomerular filtration rate
HCS	hypotensive cardiogenic shock
LVEF	left ventricular ejection fraction
NHCS	non-hypotensive cardiogenic shock
PASP	pulmonary arterial systolic pressure
SAVR	surgical aortic valve replacement
TAPSE	tricuspid annular plane systolic excursion
TAVR	transcatheter aortic valve replacement
TTE	transthoracic echocardiography
VARC-2	Valve Academic Research Consortium-2

Introduction

Management of patients with cardiogenic shock (CS) related to severe aortic stenosis (AS) is a challenging topic[1]. These patients have a poor prognosis with high morbidity and mortality (50-75%)[2,3] and a high operative risk for surgical aortic valve replacement (SAVR) (up to ≈25% operative mortality)[4]. Percutaneous balloon aortic valvuloplasty (BAV) is a therapeutic option described by Cribier et al in 1986[5], particularly for the treatment of patients with CS related to severe AS[6]. After initial enthusiasm in the 1990s, the use of BAV decreased dramatically, because of the early high restenosis rate (70%), and it was reserved for palliative indications[7].

For a decade, transcatheter aortic valve replacement (TAVR) has been an alternative to medical treatment for those who are contraindicated to surgery[8,9]. Recently, there has been renewed interest in BAV[10,11] because, as stated in the ESC guidelines for the management of valvular heart disease, "BAV may be considered as bridge to surgery or TAVR in haemodynamically unstable patients who are at high risk for surgery"[12].

However, only a few single-centre studies including small cohorts of patients with CS (n=7 to 23 patients) have been conducted[10,11,13-16], most of them before the TAVR era[13,14]. More recently, a multicentre study investigated the role of BAV in emergency conditions but did not clarify the role of BAV in patients with cardiogenic shock[17].

The purpose of the present study was to assess the periprocedural and one-year outcomes of BAV as a rescue therapy in contemporary patients with CS due to severe AS.

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Methods

PATIENT SELECTION

Between 2011 and 2016, we identified consecutive patients suffering from CS related to severe AS referred to the intensive care units of two French university centres (APHM Marseille and CHRU Lille). Each case was discussed by the institutional multidisciplinary Heart Team, which included on-call interventional cardiologists and surgeons, and on-site intensive care physicians and anaesthetists. The Heart Team agreed that a BAV should be performed as life-sustaining rescue therapy for every patient, as emergency aortic valve surgery was excluded.

In those patients, cardiogenic shock was defined as the combination of 1) a low cardiac index less than 2.2 L/min/m^2 (transthoracic echocardiography [TTE] evaluation) together with clinical signs of pulmonary congestion resistant to a high dose of intravenous loop diuretic treatment, and 2) peripheral hypoperfusion identified by the combination of several parameters including altered mental status, cold/clammy skin and extremities, oliguria with urine output of less than 30 ml/hr, or serum lactate level higher than 2.0 mmol/L.

As proposed by Menon et al from the SHOCK trial registry[18], two "subsets" of patients with CS were defined, non-hypotensive CS (NHCS) and hypotensive CS (HCS), as they are continuous pathophysiological conditions.

(i) Non-hypotensive or normotensive-hypoperfused CS is defined as above by the combination of low cardiac output/peripheral hypoperfusion together with a "normal" systolic blood pressure >90 mmHg without vasopressor circulatory support.

(ii) "Classic" CS or hypotensive CS (HCS), as in the IABP-SHOCK II trial[19], is defined as above by the combination of low cardiac output/peripheral hypoperfusion together with a low systolic blood pressure of less than 90 mmHg for more than thirty minutes or infusion of inotrope drugs needed to maintain a systolic pressure above 90 mmHg.

All patients had severe AS (indexed aortic valve area [AVA] <0.6 cm^2/m^2).

Patients with CS related to other causes such as ST-segment elevation myocardial infarction (STEMI), tamponade, stress cardiomyopathy, pulmonary embolism, myocarditis, severe aortic regurgitation, severe mitral regurgitation/stenosis, or patients with concomitant sepsis or severe bleeding were excluded. No right cardiac catheterisation or PiCCO® (Maquet, Orleans, France) was performed, but an electrocardiogram, echocardiography, biological assessments and angiocoronarography were performed before the procedure to confirm the diagnosis.

PREPROCEDURAL SCREENING

Patients received standard care therapy as previously described[20]. Invasive blood pressures were monitored with arterial and venous catheters. Patients with hypotensive CS were all catecholamine (dobutamine and/or norepinephrine)-dependent at baseline.

Severe AS was assessed according to the guidelines of the European Society of Cardiology[12].

BAV PROCEDURES

A coronarography angiogram was systematically performed before the BAV in order to exclude patients with significant left main or proximal left anterior disease.

BAV was performed using rapid pacing as previously described[6] under local anaesthesia, through the transfemoral access.

The procedure was considered successful when at least a 50% reduction of the aortic gradient was obtained without a moderate to severe aortic regurgitation[6]. This was assessed by TTE after the procedure.

CLINICAL ENDPOINTS

The primary endpoint was a composite of mortality or recurrent CS related to AS at one-year follow-up, and secondary endpoints included one-year mortality and predictive factors of the primary endpoint and one-year mortality. Other analyses included one-month mortality and post-procedural outcomes, and were described according to the Valve Academic Research Consortium-2 (VARC-2) criteria[21].

STATISTICAL ANALYSIS

Results for continuous variables were expressed as means with standard deviations when data were symmetrically distributed or otherwise as medians with ranges. The normality of distribution was assessed using the Shapiro-Wilk test and normality diagrams. Results for categorical variables were expressed as frequencies and percentages. Comparative analyses were obtained using the chi-square test for categorical data; when not applicable because of the sample size, Fisher's exact test was used. For numerical variables, we used the ANOVA test or Kruskal-Wallis test if normality of distribution was not present. Survival was graphically depicted using Kaplan-Meier curves and between-group differences were compared using the log-rank test. P-values <0.05 were considered statistically significant. Statistical analysis was performed using commercial software (SPSS version 18.0; SPSS Inc., Chicago, IL, USA).

A multivariate analysis was not possible because of the low number of patients.

Results

BASELINE PATIENT CHARACTERISTICS

We identified 44 patients (around 15% of total BAV procedures in the two institutions) with either HCS (n=31, 84% male, mean age 77.3±8.6 years) or NHCS (n=13, 53% male, mean age 77.3±7.3 years), with a global mean EuroSCORE II of 41.6±13.7%. Baseline characteristics and comorbidities are presented in **Table 1**. Other indications for BAV in our two institutions (n=250) were (i) to assess the clinical response of a reduction in aortic gradient in borderline patients prior to consideration of definitive TAVR intervention (60%), (ii) as a bridge to TAVR because of a long waiting list (40%). Details about haemodynamic evaluation and peripheral injury can be found in the **Supplementary Appendix** and **Table 2**.

PROCEDURAL DATA

In the NHCS group, BAV was performed as soon as the diagnosis of non-hypotensive CS was established, 1.2±0.5 days after admission to the intensive care unit and before starting inotropes. In the HCS group, BAV was performed 4.1±2.9 days after admission to the intensive care unit and 3.2±3.8 days after the introduction of catecholamines. No patient received mechanical circulatory support.

Table 1. Baseline patient characteristics.

Baseline characteristics	All N=44	HCS n=31	NHCS n=13	*p*-value
Clinical data				
Age (years), mean±SD	77.3±8.1	77.3±8.6	77.3±7.3	1.0
Male gender, n (%)	33 (75%)	26 (84%)	7 (54%)	0.04*
BMI (kg/m^2), mean±SD	26.9±5.6	27.1±5.9	26.6±5.1	0.78
Chronic renal failure GFR <60 mL/min, n (%)	23 (52%)	17 (55%)	6 (46%)	0.60
Dialysis, n (%)	2 (4%)	2 (6%)	0 (0%)	0.35
Prior MI, n (%)	14 (31%)	12 (38%)	2 (15%)	0.11
Prior CVA/TIA, n (%)	6 (13%)	5 (16%)	1 (8%)	0.46
COPD, n (%)	9 (20%)	5 (16%)	4 (31%)	0.27
Atrial fibrillation, n (%)	24 (54%)	16 (52%)	8 (62%)	0.55
Diabetes, n (%)	14 (31%)	10 (32%)	4 (31%)	0.92
PVD, n (%)	11 (25%)	9 (29%)	2 (15%)	0.34
Previous cardiac surgery, n (%)	3 (6%)	2 (6%)	1 (8%)	0.88
Previous CABG, n (%)	2 (4%)	1 (3%)	1 (8%)	0.52
Liver disease - cirrhosis, n (%)	3 (6%)	3 (10%)	0 (0%)	0.24
EuroSCORE II, mean±SD	41.6±13.7	45.8±13.5	31.7±8.3	0.001*
STS score, mean±SD	23.4±11.6	25.9±11.9	18.1±9.3	0.05*
Preoperative TTE				
LVEF (%), mean±SD	30±14	29±13	34±19	0.30
LV volume (ml), mean±SD	156.7±40.0	166.5±32.3	138.2±47.9	0.04*
Mean Ao gradient (mmHg), mean±SD	39.0±14.2	38.6±15.0	40.3±12.7	0.73
AVA (cm^2), mean±SD	0.61±0.17	0.65±0.15	0.54±0.18	0.06
Grade I-II AR, n (%)	19 (43%)	11 (35%)	8 (62%)	0.11
Grade I-II MR, n (%)	22 (50%)	14 (45%)	8 (62%)	0.32
PASP (mmHg), mean±SD	54.1±11.5	54.6±12.9	53.3±8.3	0.78
RV TAPSE (mm), mean±SD	14.5±3.9	14.2±3.6	15.4±4.6	0.43
RV Sdti (cm/s), mean±SD	8.7±3.2	8.6±2.9	9.1±4.2	0.71
Bicuspid aortic valve, n (%)	8 (18%)	6 (19%)	2 (15%)	0.75

*p-value <0.05. Ao: aortic; AR: aortic regurgitation; AVA: aortic valve area; BMI: body mass index; CABG: coronary artery bypass graft; CVA/TIA: cerebrovascular accident/transient ischaemic attack; COPD: chronic obstructive pulmonary disease; HCS: hypotensive cardiogenic shock; LV: left ventricular; LVEF: left ventricular ejection fraction; MI: myocardial infarction; MR: mitral regurgitation; NHCS: non-hypotensive cardiogenic shock; PASP: pulmonary artery systolic pressure; PVD: peripheral vascular disease; RV: right ventricle; STS score: Society of Thoracic Surgeons score; TAPSE: tricuspid annular plane systolic excursion; TTE: transthoracic echocardiography

Thirty-nine (88%) procedures were considered successful with a significant reduction of the aortic gradient. The immediate haemodynamic changes produced by BAV are shown in **Supplementary Table 1**. Postoperative TTE evaluation showed a significant overall decreased mean transaortic gradient (from 39.9±14.2 mmHg to 25.3±11.2 mmHg; p=0.01) and increased AVA (from 0.61±0.17 cm^2 to 0.82±0.20 cm^2; p=0.01).

OUTCOMES

i) In-hospital (Supplementary Table 2) and one-month outcomes (Supplementary Table 3)

Three patients (13%) died during the procedure (n=2 [6%] in the HCS subgroup and n=1 [7%] in the NHCS subgroup)

Table 2. Baseline haemodynamic and biological evaluations.

	All N=44	HCS n=31	NHCS n=13	*p*-value
Clinical parameters				
Heart rate/min, mean±SD	94.9±7.6	92.8±15.6	99.5±21.5	0.30
Mechanical ventilation, n (%)	6 (13%)	5 (16%)	1 (8%)	0.46
Cardiac index (TTE)				
Pre-BAV cardiac index (l/min/m²), mean±SD	1.60±0.78	1.38±0.74	1.90±0.54	0.01*
Preoperative medication and score				
Dobutamine dose (microg/kg/min), mean±SD	5.8±5.4	8.2±4.9	0.0±0.0	0.001*
Norepinephrine dose (mg/hr), mean±SD	1.0±2.3	1.5±2.7	0.0±0.0	0.05*
Loop diuretic dose (mg/24 hrs), mean±SD	1,405±302	1,430±265	1,354±376.3	0.48
VIS score, mean±SD	25.6±44.6	36.3±49.5	0.0±0.0	0.01*
SOFA score, mean±SD	6.0±2.9	6.9±1.8	4.0±1.2	0.001*
Preoperative biological data				
Creatinine (mg/l), mean±SD	19.1±9.1	19.4±8.8	18.7±10.3	0.83
Troponin T Hs (ng/l), mean±SD	343.4±567.8	392.1±629.5	136.1±133.7	0.24
NTproBNP, mean±SD	18,151±21,008	18,375±23,652	17,444±10,185	0.93
Lactate (mg/l), mean±SD	269.9±157.8	281.3±160.5	150.5±41.7	0.27
Factor V (%), mean±SD	54.4±32.5	52.1±32.6	64.3±35.6	0.47
PT (%), mean+/SD	63.3±20.0	60.3±20.6	71.6±16.8	0.12
Haemoglobin (g/dl), mean±SD	10.9±1.8	10.9±1.9	11.1±1.6	0.81
CRP (mg/l), mean±SD	57.6±55.2	56.6±64.2	41.6±50.2	0.24

*p-value <0.05. BAV: balloon aortic valvuloplasty; CRP: C-reactive protein; Hb: haemoglobin; HCS: hypotensive cardiogenic shock; NHCS: non-hypotensive cardiogenic shock; PT: prothrombin time; SOFA score: sequential organ failure assessment score; TTE: transthoracic echocardiography; VIS score: vasoactive-inotropic score

due to a tamponade (n=1), severe aortic regurgitation (n=1), or haemodynamic collapse (n=1). Four patients (13%) with an efficient procedure were successfully weaned from inotropic support within the first 72 hours after the procedure in the hypotensive CS group. The total hospital mortality rate was 45% (n=20), n=16 in the HCS subgroup and n=4 in the NHCS subgroup (p=0.20). Twelve patients (27%) were discharged home before two weeks after BAV, n=4 (13%) in the HCS subgroup and n=8 (62%) in the NHCS subgroup (p=0.001). There were no major vascular complications or life-threatening bleedings, but n=3 (7%) major bleeding and n=2 (4%) minor bleeding. No patients were on dialysis at the time of BAV. Five patients (11%) required haemodialysis after the procedure **(Supplementary Table 2)**. Intra-hospital mortality was significantly lower in patients with a successful procedure (n=13 [33%] vs. n=4 [80%]; p=0.04). Similarly, surviving patients had a lower post-procedural transaortic maximal velocity (2.9±0.9 m/s vs. 3.5±0.5 m/s; p=0.05) and a lower post-procedural transaortic mean gradient (22.5±9.7 vs. 30.5±12.6 mmHg; p=0.03).

A vasoactive-inotropic (VIS) score ≥10 (n=13 [76%] vs. n=8 [29%]; p=0.002) or a sequential organ failure assessment (SOFA) score ≥7 (n=15 [93%] vs. n=6 [21%]; p<0.001) was highly predictive of one-month mortality after BAV.

The mortality rate at one month reached 47% (n=21). Causes of death before and after one month are presented in **Supplementary Table 4**.

During the follow-up, n=12 (27%) patients had either a staged TAVR (n=10) or SAVR (n=2) with a median delay of 79±49 days after BAV, n=6 (19%) in the HCS group and n=6 (46%) in the NHCS group (p=0.06). Among the 12 patients who finally underwent TAVR or SAVR, n=4 (33%) were dead at one year. Follow-up after BAV for the entire cohort (n=44) is shown in **Figure 1**.

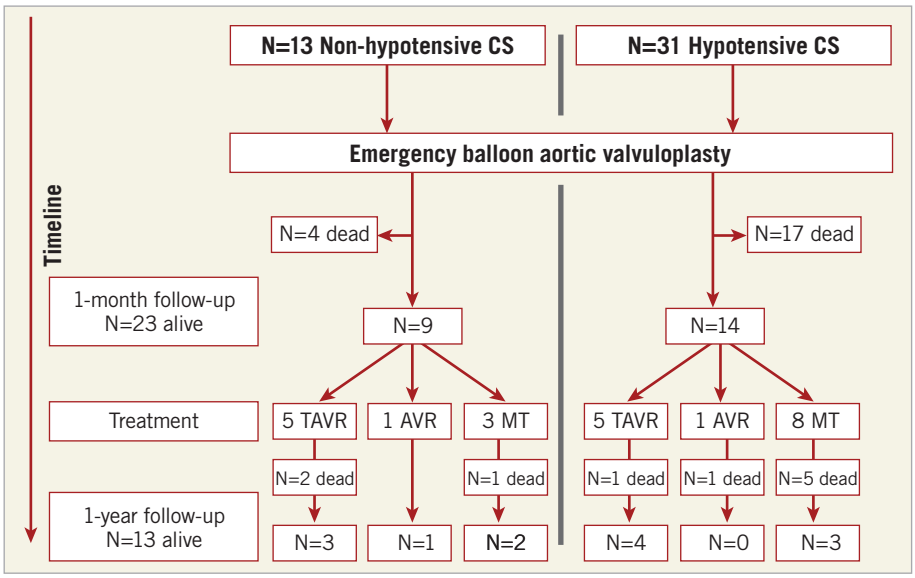

Figure 1. *Follow-up after percutaneous balloon aortic valvuloplasty (BAV). AVR: aortic valve replacement; MT: medical treatment; TAVR: transcatheter aortic valve replacement*

ii) One-year outcomes (Supplementary Table 3)

At one year, the rate of composite all-cause death or recurrent CS was 75% (n=33) and was significantly higher in the HCS subgroup (n=26 [83%] vs. n=7 [53%]; p=0.03). The mortality rate at one-year follow-up was 70% (n=31) in the overall cohort with a trend for better prognosis in the NHCS subgroup (mortality in HCS n=24 [77%] and in NHCS n=7 [53%]; p=0.11). One-year cumulative survival also showed a trend for better prognosis for the NHCS population with a log-rank p=0.09 **(Figure 2)**.

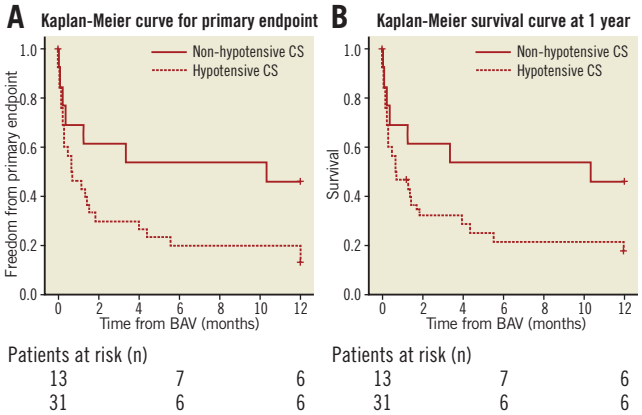

Figure 2. *NHCS and HCS survival. A) Kaplan-Meier curve for the primary endpoint of patients undergoing BAV for hypotensive CS (HCS) and non-hypotensive CS (NHCS) due to severe aortic stenosis (log-rank p=0.05). B) Kaplan-Meier survival curve of patients undergoing BAV for hypotensive CS (HCS) and non-hypotensive CS (NHCS) due to severe aortic stenosis (log-rank p=0.09).*

PREDICTIVE FACTORS OF THE PRIMARY ENDPOINT AND ONE-YEAR MORTALITY

In the global cohort, univariate predictive factors of the primary endpoint included a preoperative dose of dobutamine >5 microg/kg/min (100% vs. 57%; p=0.001) and delayed BAV >48 hrs (90% vs. 59%; p=0.01). Likewise, the predictive factors for one-year mortality were a preoperative dose of dobutamine >5 microg/kg/min (94% vs. 53%; p=0.02) and delayed BAV >48 hrs (86% vs. 54%; p=0.02). The prognosis of the three populations – NHCS, HCS with BAV ≤48 hrs and HCS with BAV >48 hrs – differed significantly at one-year follow-up regarding the primary endpoint (log-rank p=0.01) and survival (log-rank p=0.04) **(Figure 3)**.

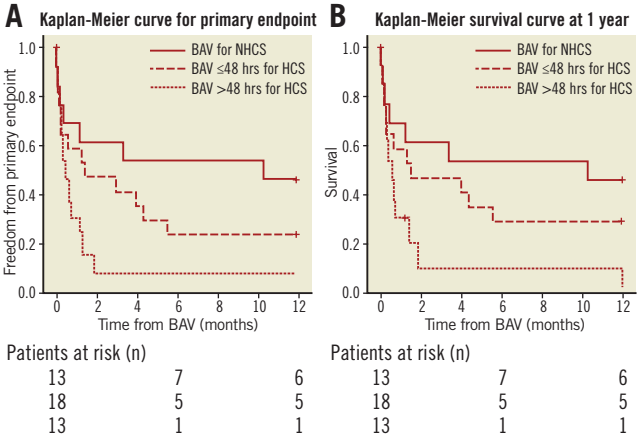

Figure 3. *Timing of BAV. A) Kaplan-Meier curve for the primary endpoint of patients with BAV for NHCS, BAV ≤48 hrs for HCS, or BAV >48 hrs for HCS (log-rank p=0.01). B) Kaplan-Meier survival curve at one year for patients with BAV for NHCS, BAV ≤48 hrs for HCS, or BAV >48 hrs for HCS (log-rank p=0.04).*

Discussion

The present study, including 44 patients and conducted in two centres, is one of the largest published cohorts of patients undergoing BAV for cardiogenic shock related to a severe AS **(Table 3)**. It discloses four key findings: (1) mortality at one year in contemporary patients remains high (70%), (2) mortality is directly related to the duration of shock before performing BAV, (3) more specifically, initiation of inotropic agents appears to be a critical time point, with a short time window (<48 hrs) after which conducting BAV becomes associated with a dire outcome, (4) the most favourable situation to perform BAV appears to be before the introduction of catecholamines, as it allows bringing 50% of patients to staged TAVR or AVR.

MORTALITY HAS NOT IMPROVED OVER THE YEARS

We have not seen any improvement regarding early mortality since 1994 **(Table 3)**. In the modern era of TAVR, we confirm that BAV for CS remains associated with a dramatically poor prognosis,

Table 3. Summary of BAV and CS studies.

	Study design	N	Age (years)	Mean aortic gradient (mmHg)	LVEF (%)	Catecholamine dose known?	One-month mortality	Ref.
Moreno et al 1994	Single centre	21	74±3	49±4	29±3	No	43%	13
Buchwald et al 2001	Single centre	14	74±11	?	?	No	71%	14
Hamid et al 2010	Single centre	7	77±12	?	28±10	No	?	10
Saia et al 2013	Single centre	23	77±10	?	?	?	56%	15
Theiss et al 2014	Single centre	18	78±1	?	32±3	No	27%	16
Olasinska et al 2016	Single centre	7	72±11	?	?	No	?	11
Debry et al 2018	Two centres	44	77±8	39±14	30±14	Yes	47%	–

with only 27% of patients able to be treated by either TAVR or SAVR within the year, and 70% mortality at one year.

For the first time, we report that NHCS patients have a lower risk of death or recurrent CS at one year than the HCS subgroup (p=0.03) and that there is a trend towards lower mortality in that population at one month (p=0.14) and at one year (p=0.09). BAV may be useful for NHCS patients since it allows performing staged SAVR or TAVR in half of the cases.

Old studies included smaller cohorts of patients and details about haemodynamic monitoring were scarce. In particular, biological data regarding renal or hepatic failure and catecholamine doses at the time of valvuloplasty are lacking[13,14]. Even a recent study does not give much information about medical shock management and outcomes after BAV[16]. Trials exploring the outcomes of emergency TAVR for cardiogenic shock related to AS seem to have the same weakness[22,23]. Nevertheless, we report a one-month mortality rate of 47%, consistent with previous studies with in-hospital or one-month mortality varying from 43%[13] to 71%[14].

KEY ROLE OF THE TIME OF BAV RELATIVE TO INOTROPE SUPPORT

Our results illustrate the difficulty of improving the outcomes of patients in CS related to a severe AS. Duration of shock symptoms before causal treatment (to relieve valve obstruction), if attempted, seems to determine outcome. We show that the time of introduction of inotropic agents is crucial, since patients without amines (NHCS) have a better prognosis at one year. The valvuloplasty should be addressed as soon as signs of impaired end-organ perfusion appear, instead of starting inotropic agents.

When catecholamines have been initiated, a delay in performing BAV can be deadly. Performing an early BAV, during the first 48 hours, before for example increasing dobutamine dose beyond 5 microg/kg/min to maintain a systolic pressure above 90 mmHg, could be the answer to rapid deterioration of haemodynamic status. A delayed BAV after 48 hours may be useless, as hepatic and renal failure worsens. In a much smaller series (n=14), Buchwald et al also suggested a beneficial effect of an early BAV within the first 48 hours of shock diagnosis[14].

IS IT TIME FOR 24 HRS A DAY "URGENT TAVR"?

Because one-year mortality remains high in AS patients with CS treated with BAV (47% in the present study), we can legitimately ask about the potential of emergency TAVR in the management of these patients. However, a retrospective study of patients (n=27) with AS and CS treated by emergency TAVR reported a 30-day and one-year mortality rate of 33% and 41%, respectively[22]. Another recent multicentre study investigating emergent TAVI and BAV (n=118) also showed high immediate procedural and 30-day mortality (33%), with more stroke and vascular complications for the TAVI group as compared to the BAV group[17].

Altogether, this may suggest that emergent TAVR is not the ultimate option in AS patients with cardiogenic shock. Still, our data may suggest that to organise centres to perform emergent BAV in these patients would save lives.

Limitations

This was not a randomised trial and the low number of patients with cardiogenic shock prohibited multivariate analysis of factors impacting on 30-day survival. However, the selection of patients was very stringent and included an extensive screening (ECG, biology, echography and coronarography) allowing the exclusion of CS with uncertain aetiology or non-related to pure aortic stenosis. We believe that this very well characterised population may help to define predictive factors of mortality in this very difficult situation and thus help to define "when" and "for which patients" this procedure may be more beneficial. These data must be confirmed in large prospective multicentric cohorts.

Conclusions

Despite the initial success of urgent BAV, morbidity and mortality of CS related to severe AS remains dramatically high and is directly related to the duration of shock. Performing BAV before starting inotropic agents or within 48 hours of their initiation appears to be key to survival. With the improvement of the outcomes of TAVR, there is a need for a randomised trial comparing urgent BAV followed by staged TAVR and emergency TAVR for these unstable patients.

Impact on daily practice

Despite the initial success of urgent BAV, morbidity and mortality of CS related to severe AS remains dramatically high and is directly related to the duration of shock. Performing BAV before starting inotropic agents or within 48 hours of their initiation appears to be key to survival.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix. Results.

Supplementary Table 1. BAV procedural data.

Supplementary Table 2. In-hospital outcomes according to VARC-2 criteria and postoperative data.

Supplementary Table 3. One-month and one-year outcomes.

Supplementary Table 4. Causes of death before and after one-month follow-up.

The supplementary data are published online at: http://www.pcronline.com/eurointervention/138th_issue/92

Supplementary data

Supplementary Appendix. Results

Severe aortic stenosis

All patients had a severe AS **(Table 1)**, with a mean aortic gradient of 39.0±14.2 mmHg (HCS=38.6±15.0 mmHg; NHCS=40.3±12.7 mmHg; p=0.72), and a mean aortic valve area of 0.61±0.17 cm^2 (HCS=0.65±0.15 cm^2; NHCS=0.54±0.18 cm^2; p=0.06). Mean LVEF was 30±14% (HCS=29±13%; NHCS=34±19%; p=0.30).

Haemodynamic evaluation

Mean cardiac index evaluated by TTE was very low (1.60±0.78 L/min/m^2). In the HCS subgroup, high doses of catecholamines were used at the time of BAV: mean dobutamine dose of 8.2±4.9 micrograms/kg/min (p=0.001), and mean norepinephrine dose of 1.5±2.7 mg/hr (p=0.05). Impaired end-organ perfusion was observed at the time of the procedure for all patients with (i) severe renal failure (mean creatinine=19.1±9.1 mg/l), (ii) hepatic injury (mean prothrombin time=63.3±20.0% and mean factor V=54.4±32.5%), (iii) cardiac injury (mean troponin T Hs=343.4±567 ng/l) and (iv) anaerobic metabolism (lactate=269±157 mg/l) **(Table 2)**.

Supplementary Table 1. BAV procedural data.

Procedural data	All N=44	HCS n=31	NHCS n=13	*p*-value
Delay between catecholamine introduction and BAV, mean±SD	2.3±3.4	3.2±3.8	0.0±0.0	**0.002***
Procedural success, n (%)	39 (88%)	27 (87%)	12 (92%)	0.62
Balloon diameter (mm), mean±SD	22.4±1.7	22.4±1.6	22.5±2.1	0.86
BAV sheath size (Fr), mean±SD	11.6±0.9	11.7±0.7	11.3±1.3	0.15
Number of inflations, mean±SD	1.7±0.6	1.6±0.6	1.9±0.7	0.28
Local anaesthesia, n (%)	38 (83%)	26 (83%)	12 (92%)	0.46
Pre-closure device, n (%)	24 (54%)	16 (51%)	8 (61%)	0.54
Manual compression, n (%)	20 (45%)	15 (49%)	5 (39%)	0.54
Proc fluotime (sec), mean±SD	602±284	637±279	534±299	0.33
TTE mean Ao gradient (mmHg) before BAV, mean±SD	39.0±14.2	38.6±15.0	40.3±12.7	0.73
TTE mean Ao gradient (mmHg) after BAV, mean±SD	23.3±11.2	22.5±10.7	25.4±12.5	0.46
TTE grade III-IV AR, n (%)	1 (2%)	1 (2%)	0 (0%)	0.51

* *p*-value <0.05.
Procedural success: when at least 50% reduction of the aortic gradient was obtained without a moderate to severe aortic regurgitation, which was assessed by TTE after the procedure.
Ao: aortic; BAV: balloon aortic valvuloplasty; fluotime: fluoroscopy time; HCS: hypotensive cardiogenic shock; NHCS: non-hypotensive cardiogenic shock; Proc: procedural; TTE: transthoracic echocardiography

Supplementary Table 2. In-hospital outcomes according to VARC-2 criteria and postoperative data.

Outcomes	All N=44	HCS n=31	NHCS n=13	*p*-value
Clinical data	-	-	-	-
In-hospital mortality, n (%)	20 (45%)	16 (52%)	4 (31%)	0.20
Procedural mortality, n (%)	3 (6%)	2 (6%)	1 (8%)	0.88
Major vascular complication, n (%)	0 (0%)	0 (0%)	0 (0%)	1.0
Blood transfusion (units), mean±SD	0.9±1.6	1.3±1.9	0.3±1.2	0.13
Stroke, n (%)	1 (2%)	1 (3%)	0 (0%)	0.51
TIA, n (%)	0 (0%)	0 (0%)	0 (0%)	1.0
Pacemaker implantation, n (%)	0 (0%)	0 (0%)	0 (0%)	1.0
Acute kidney injury 3, n (%)	9 (20%)	7 (23%)	2 (15%)	0.57
Need of haemodialysis, n (%)	5 (11%)	4 (13%)	1 (8%)	0.62
Cardiac tamponade, n (%)	1 (2%)	0 (0%)	1 (8%)	0.12
Stay ICU (days), mean±SD	9.9±8.9	11.5±9.1	6.1±7.6	0.08
Stay duration (days), mean±SD	18.2±11.9	18.3±12.4	18.1±10.9	0.96
Discharge home after ICU, n (%)	12 (27%)	4 (13%)	8 (62%)	**0.01***
Postoperative TTE	-	-	-	-
LVEF (%), mean±SD	31.8±16.3	29.5±11.5	36.8±23.3	0.21
Mean Ao gradient (mmHg), mean±SD	23.3±11.2	22.5±10.7	25.4±12.5	0.46
AVA (cm^2), mean±SD	0.82±0.20	0.79±0.15	0.86±0.27	0.47
Grade III-IV AR, n (%)	1 (2%)	1 (2%)	0 (0%)	0.51
RV TAPSE (mm), mean±SD	15.2±3.3	15.3±3.8	15.2±2.7	0.93
RV Sdti (cm/s), mean±SD	9±2	9±2	9±1	1.00
PASP (mmHg), mean±SD	45.4±16.7	46.8±13.7	43.8±20.9	0.71
Postoperative biological data	-	-	-	-
Lactate max (mg/l), mean±SD	255.3±169.5	273.2±175.1	136.7±12.9	0.20
Troponin T Hs max (ng/l), mean±SD	834.8±1,285.2	905.4±1,367.7	552.6±948.9	0.59
Creatinine max (mg/l), mean±SD	25.2±12.3	26.7±12.4	21.3±12.0	0.24
Haemoglobin nadir (g/dl), mean±SD	9.8±1.8	9.7±1.9	10.0±2.0	0.77

* *p*-value <0.05.
AR: aortic regurgitation; AVA: aortic valve area; HCS: hypotensive cardiogenic shock; ICU: intensive care unit; LVEF: left ventricular ejection fraction; max: maximum; NHCS: non-hypotensive cardiogenic shock; PASP: pulmonary artery systolic pressure; NHCS: non-hypotensive CS; RV: right ventricle; TAPSE:

tricuspid annular plane systolic excursion; TIA: transient ischaemic attack; TTE: transthoracic echocardiography

Supplementary Table 3. One-month and one-year outcomes.

Follow-up after BAV	All N=44	HCS n=31	NHCS n=13	*p*-value
1-month outcomes	-	-	-	-
1-month mortality, n (%)	21 (47%)	17 (55%)	4 (31%)	0.14
1-month stroke/TIA, n (%)	1 (2%)	1 (3.2%)	0 (0%)	0.52
1-month recurrent heart failure, n (%)	5 (11%)	5 (16%)	0 (0%)	0.12
1-month NYHA IV, n (%)	2 (4%)	2 (6%)	0 (0%)	0.32
Staged procedures during FU	-	-	-	-
TAVR, n (%)	10 (22%)	5 (16%)	5 (38%)	**0.01***
SAVR, n (%)	2 (4%)	1 (3%)	1 (8%)	0.52
1-year outcomes	-	-	-	-
1-year mortality, n (%)	31 (70%)	24 (77%)	7 (53%)	0.11
1-year mortality or recurrent CS, n (%)	33 (75%)	26 (83%)	7 (53%)	**0.03***

* *p*-value <0.05.
CS: cardiogenic shock; FU: follow-up; HCS: hypotensive cardiogenic shock; NHCS: non-hypotensive cardiogenic shock; SAVR: surgical aortic valve replacement; TAVR: transcatheter aortic valve replacement; TIA: transient ischemic attack

Supplementary Table 4. Causes of death before and after 1-month follow-up.

Causes of death after BAV	Before 1-month FU n=21 deaths	After 1-month FU n=10 deaths
Refractory cardiogenic shock, n (%)	8 (38%)	2 (20%)
Haemorrhagic shock, n (%)	2 (9%)	0 (0%)
Septic shock, n (%)	1 (5%)	0 (0%)
Recurrent heart failure, n (%)	0 (0%)	2 (20%)
Myocardial infarction, n (%)	1 (5%)	1 (10%)
Acute kidney injury, n (%)	2 (9%)	0 (0%)
Pneumonia, n (%)	3 (15%)	2 (20%)
Tamponade, n (%)	1 (5%)	0 (0%)
Cancer, n (%)	0 (0%)	2 (20%)
Severe aortic regurgitation, n (%)	1 (5%)	0 (0%)
Unknown, n (%)	2 (9%)	1 (10%)

FU: follow-up