

Transcatheter interventions for left-sided valvular heart disease complicated by cardiogenic shock: a consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) in collaboration with the Association for Acute Cardiovascular (ACVC) and the ESC Working Group on Cardiovascular Surgery.

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HAL Id: hal-04196088 https://univ-rennes.hal.science/hal-04196088v1

Submitted on 30 Nov 2023

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▶ To cite this version:

Chiara Fraccaro, Nicole Karam, Helge Möllmann, Sabine Bleiziffer, Nikolaos Bonaros, et al.. Transcatheter interventions for left-sided valvular heart disease complicated by cardiogenic shock: a consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) in collaboration with the Association for Acute Cardiovascular (ACVC) and the ESC Working Group on Cardiovascular Surgery.. EuroIntervention: journal of EuroPCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology, 2023, 19 (8), pp.634-651. 10.4244/EIJ-D-23-00473 . hal-04196088



TRANSCATHETER INTERVENTIONS FOR LEFT-SIDED VALVULAR HEART **DISEASE COMPLICATED BY CARDIOGENIC SHOCK: A consensus statement** from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) in collaboration with the Association for Acute CardioVascular Care (ACVC) and the ESC Working Group on Cardiovascular Surgery

7 Short title: Left-sided structural intervention for cardiogenic shock

8 9 Total word count: 4992

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1 Abstract

- 2 Valvular heart disease (VHD) is one of the most frequent causes of heart failure (HF) and
- 3 is associated with poor prognosis particularly among patients with conservative
- 4 management. Development and improvement of catheter-based VHD interventions have
- 5 broadened the indications for transcatheter valve interventions from inoperable-high risk
- 6 patients to younger/lower risk patients. Cardiogenic shock (CS) associated with severe
- 7 VHD is a clinical condition at very high risk of mortality where surgical treatment is often
- 8 deemed prohibitive risk. Transcatheter valve interventions might be a promising alternative
- 9 in this setting given their less invasiveness. However, supportive scientific evidence is
- scarce, and often limited to small case series. Current guidelines on VHD do not contain
- specific recommendations on how to manage patients with VHD and CS. The purpose of this clinical consensus statement, developed by a group of international experts invited by
- the European Association of Percutaneous Cardiovascular International experts in
- 14 Scientific Documents and Initiatives Committee, is to perform a revision of available
- 15 scientific evidences on the management of CS associated with left-sided VHD, and to
- 16 provide a rationale and practical approach for the application of transcatheter valve
- 17 interventions in this specific clinical setting.
- 18

19 Classification: Expert Consensus

20

21 Keywords. Valvular heart disease; cardiogenic shock; transcatheter valve interventions;

- 22 aortic valve disease; mitral valve disease; structural heart disease.
- 23





1 Abbreviation list

| AMI | Acute myocardial infarction |
|---------|---|
| AR | aortic regurgitation |
| AS | aortic stenosis |
| BAV | balloon aortic valvuloplasty |
| BVF | bioprosthetic valve failure |
| CAD | coronary artery disease |
| СО | cardiac output |
| CS | cardiogenic shock |
| EACTS | European Association for Cardio-Thoracic Surgery |
| EAPCI | European Association of Percutaneous Cardiovascular Interventions |
| ESC | European Society of Cardiology |
| HF | heart failure |
| HVD | haemodynamic valve deterioration |
| IABP | intra-aortic balloon pump |
| ICA | invasive coronary angiography |
| LA | Left atrium/atrial |
| LV | left ventricular |
| LVEF | left ventricular ejection fraction |
| MCS | mechanical circulatory support |
| MR | mitral regurgitation |
| MS | mitral stenosis |
| MSCT | multislice computed tomography |
| PVL | paravalvular leak |
| PCI | percutaneous coronary intervention |
| PMBV | percutaneous mitral balloon valvuloplasty |
| RCT | randomized controlled trial |
| SCAI | Society for Cardiovascular Angiography and Interventions |
| SVD | structural valve deterioration |
| TAVI | transcatheter aortic valve implantation |
| TEER | transcatheter edge-to-edge repair |
| TMVI | transcatheter mitral valve implantation |
| TEE | transoesophageal echocardiography |
| TTE | trans-thoracic echocardiography |
| VA-ECMO | venous-arterial extracorporeal membrane oxygenation |
| VHD | valvular heart disease |





1 INTRODUCTION

2 Valvular heart disease (VHD) is among the most frequent causes of heart failure (HF), associated with poor prognosis, particularly when managed conservatively.^{1,2} Acute 3 valvular emergencies comprise approximately 8% of coronary care unit admissions,³ but it 4 is unclear how many turn from acute HF to cardiogenic shock (CS).^{4–7} Transcatheter valve 5 6 interventions provided treatment options for a subset of patients with VHD at prohibitive 7 or very high surgical risk. Moreover, technological advances broadened their indication to younger or lower risk patients, or even to less symptomatic or moderate VHD.8 8 9 Conversely, patients with VHD and CS are generally excluded from randomized controlled 10 trials (RCT) exploring these technologies, and less evidence is available in this setting. 11 Therefore, the 2021 European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS) Guidelines for VHD ⁹ did not include specific sections 12 13 for VHD presenting with CS. Treatment strategies are left to the discretion of 14 multidisciplinary Heart Teams in a case-by-case fashion, weighing risks and benefits to 15 identify those likely to benefit from interventions and avoid futility. 16 The purpose of this consensus statement, developed by international experts invited by the European Association of Percutaneous Cardiovascular Interventions (EAPCI) 17 18 Scientific Documents and Initiatives Committee, is to provide a practical approach to 19 transcatheter valve interventions use in patients with left-sided VHD and CS, based on available scientific evidences. 20

21

22 DEFINITION OF CARDIOGENIC SHOCK



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| 1 | Cardiogenic shock (CS) is a clinical syndrome characterized by life-threatening |
|----|--|
| 2 | organ hypoperfusion, caused by low cardiac output (CO) due to primary cardiac pump |
| 3 | failure despite adequate volume preload. ^{10–14} Variable definitions of CS exist |
| 4 | (Supplemental Table 1). Consistent part of CS evidence stems from patients with acute |
| 5 | myocardial infarction (AMI), while other aetiologies are increasing. ¹⁵ The Society for |
| 6 | Cardiovascular Angiography and Interventions (SCAI) recently published a disease |
| 7 | severity classification in an effort to make CS patients more comparable for clinical and |
| 8 | research purposes. ^{16,17} |
| 9 | We defined CS associated with VHD as significant VHD combined with systolic blood |
| 10 | pressure <90 mmHg for >30 min OR need of vasopressors to maintain systolic blood |
| 11 | pressure >90 mmHg, elevated serum lactate levels and clinical signs of end-organ |
| 12 | hypoperfusion (including cool, sweated extremities, altered mental status, oliguria), |
| 13 | corresponding to SCAI stage $\geq C$. |
| 14 | |
| 15 | CLINICAL SCENARIOS OF CS AND VHD |
| 16 | Acute onset of new severe VHD |

17 CS may be due to acute onset of severe VHD such as ischaemic mitral regurgitation (MR), 18 often related to AMI. Functional MR due to left ventricular (LV) global or regional 19 remodelling or ischaemic papillary muscle dysfunction, may resolve after revascularization 20 and recovery of LV function, or persist and require treatment. Acute MR may also be 21 related to chord rupture. Acute severe AR, commonly leads to CS,^{18,19}and is caused by 22 type A aortic dissection, rupture of fenestrated aortic valve or endocarditis, typically 23 requiring surgical correction¹⁹. Other rare situations are iatrogenic or traumatic aortic valve





- 1 injury, or AR in LV assist device patients. Acute severe VHD may also be related to
- 2 bioprosthetic valve failure (BVF).^{19,20}
- 3

4 **Deterioration of chronic VHD**

5 Pre-existing moderate to severe clinically stable VHD (can turn into acute decompensated
6 HF and CS with various cardiac or non-cardiac triggers.

In BVF, patients in CS should have at least severe haemodynamic valve deterioration (HVD)
(i.e. stage 3)²¹ for valve-related haemodynamic instability. All causes of BVF may lead to
severe HVD, including 1) structural valve deterioration (SVD) (i.e., cusp tear); 2) nonstructural valve dysfunction (i.e., paravalvular leak); 3) thrombosis; or 4) endocarditis
(figure 1).

Primary approach should address the triggering condition. However, transcatheter
interventions can be used as bailout in complex cases or when the trigger, such as pregnancy,
persists.

15

16 <u>Cardiovascular triggers</u>

a. *Atrial fibrillation and other (supra-)ventricular arrhythmias:* While left-sided VHD
precipitate atrial fibrillation occurrence, the latter complicates moderate to severe left-sided
valvular stenosis. In the SEAS trial, at 4-year follow-up, 6% of patients with mild to
moderate aortic stenosis (AS) developed atrial fibrillation.²² In AS and mitral stenosis
(MS), rapid heart rate and loss of the atrial contraction limit the filling time of the LV.
Restoration of sinus rhythm is crucial, though difficult to achieve, particularly in MS.





| 1 | b. <i>AMI:</i> AS is not uncommon in AMI patients, and this combination is independently |
|----|---|
| 2 | associated with short and long-term mortality .23 Impaired ischaemic LV contractility |
| 3 | further reduces CO, and AS increases afterload creating a vicious circle, leading to CS. |
| 4 | Treatment is challenging because inotropic drugs and diuretics increase intraventricular |
| 5 | pressure increasing haemodynamic impairment and gradient. |
| 6 | c. <i>Hypertensive crisis</i> and rapid <i>volume overload</i> (intravascular intravenous fluid |
| 7 | infusion or blood transfusion) can also cause CS in severe VHD but can generally be |
| 8 | treated medically. |
| 9 | d. <i>Takotsubo syndrome</i> has been associated with pulmonary oedema in AS^{24} . |
| 10 | Moreover, dynamic LV outflow tract obstruction typical of apical ballooning may be |
| 11 | create severe MR through systolic anterior motion of the anterior mitral leaflet, which may |
| 12 | result in CS. ²⁵ As with AMI, medical treatment is challenging and may aggravate |
| 13 | haemodynamic impairment and CS in AS. Conversely, cautious use of beta-blockers |
| 14 | (ideally starting with intravenous, short acting beta-clockers like esmolol) with fluid |
| 15 | resuscitation, reduces LV outflow tract obstruction by decreasing basal hypercontractility, |
| 16 | increasing LV filling and size, and reducing heart rate, all potentially leading to MR |
| 17 | reduction and haemodynamic stabilization. ²⁶ |
| | |

18

19 <u>Non-cardiovascular triggers</u>

a. *Pregnancy* carries high risk of cardiac decompensation in VHD due to pregnancyrelated haemodynamic changes. Stenotic VHD, particularly MS, are generally less
tolerated during pregnancy than regurgitant lesions, as increased heart rate, stroke volume
and CO increase transvalvular gradient by approximately 50%, mainly between the first





and second trimesters, worsening patient's and foetus' prognosis.²⁷⁻³¹ Accordingly, MS
 should be treated pre-conceptionally when diagnosed. Otherwise, transcatheter valve
 interventions provide minimally invasive options for acutely decompensated condition not
 responsive to medical treatment³².

b. Severe infection/sepsis can lead to decreased systemic vascular resistance and
hypovolemia, causing compensatory increase in heart rate and hypotension despite
increased CO, poorly tolerated in severe MS or AS. Besides, decreased preload increases
valvular gradients, aggravating pre-existing stenosis. Cardiovascular comorbidities are risk
factors for septic shock,³³ while infection is the main non-cardiac deaths cause (up to 31%)
in AS.³⁴⁻³⁶

In most patients with septic non-CS, VHD is a bystander and won't require specific urgent
intervention. However, valvular intervention might be advisable for selected patients when
standard medical therapy fails or weaning and recovery seem challenging. Emergency
percutaneous mitral balloon valvuloplasty (PMBV) has been effective in this context.³⁷

15 Balloon valvuloplasty avoids prosthetic valve implantation in infected patients at

16 endocarditis risk. However, it carries an acute MR or AR risk. Weighing the risk-benefit is

17 challenging, and decision should be tailored to patient's condition.

18 a. *Other precipitating factors* include severe anaemia, acute renal failure,

19 hyperthyroidism and hypoalbuminemia, all usually improving after treatment and not

20 requiring emergent valve intervention.

21

22 EMERGENT DIAGNOSTIC WORKUP

23 Non-invasive diagnostic tools





| 1 | Transthoracic echocardiography (TTE). TTE is the optimal modality in CS, ³⁸ determining |
|----|--|
| 2 | the cause and severity of underlying VHD and their potential accountability. Limited |
| 3 | point-of-care cardiac ultrasound focusing on 2-dimensional assessment of LV function, |
| 4 | such as LVEF, may miss important VHD lesions ³⁹ . Discrimination of the severity of VHD |
| 5 | using TTE requires high image quality, precise measurement, complex calculations, and |
| 6 | integration of multiple criteria. Moreover, the low flow status of CS should be accounted |
| 7 | for, as it might underestimate transvalvular gradients. Conversely, medications used in CS, |
| 8 | such as dobutamine, might increase transvalvular gradient, over-estimating VHD. We |
| 9 | herein propose an echocardiographic assessment workflow in CS (Figure 2, Table 1). |
| 10 | |
| 11 | Transoesophageal echocardiography (TEE). TEE may increase diagnostic accuracy, |
| 12 | especially in case of poor acoustic TTE window, and is relatively straightforward to |
| 13 | perform in patients under mechanical ventilation. TEE may identify BVF aetiology, |
| 14 | differentiate PVL from valvular regurgitation, and help in suspected endocarditis. It is |
| 15 | mandatory for transcatheter mitral valve therapies to evaluate eligibility and guide |
| 16 | intervention. It may be used for aortic valve sizing, if CT scan is not available (Table 1). |
| 17 | |
| 18 | Multislice computed tomography (MSCT). MSCT is complementary to TTE. Calcium |
| 19 | scoring using non-contrast MSCT can confirm AS severity (likely if >2000 AU in men and |
| 20 | >1200 AU in women) in discordant AS grading (aortic valve area <1cm ² and mean |
| 21 | gradient <40mmHg) related to low CO. MSCT with contrast injection is the gold standard |
| 22 | for feasibility study and planning of valvular interventions, such as transcatheter aortic |
| 23 | valve implantation (TAVI). MSCT acquisition protocol should include contrast enhanced |
| | |



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1 ECG-gated or triggered heart and aortic root scan, and non-ECG gated vascular bed scan 2 from subclavian arteries to superficial femoral arteries, reconstructed at 1.0mm or less slice 3 thickness for accurate multiplanar evaluations (at least 64-detector technology). 4 High spatial resolution of MSCT by multiplanar and 3D-volume reconstructions, provide 5 accurate analysis of valve morphology (tricuspid, vs bicuspid, calcium distribution), aortic 6 root anatomy, vascular access route, and coronary arteries, the latter being challenging in 7 CS due to tachycardia and low CO. Contrast-enhanced MSCT is also useful in BVF to 8 discriminate SVD, thrombosis, pannus and infective endocarditis, and in planning valve-9 in-valve procedures (Table 1). 10

11 Invasive diagnostic tools

12 Invasive coronary angiography (ICA)., CAD is diagnosed in 20 to 80% of symptomatic severe AS according to age group, and increases operative risk⁴⁰ Besides, among patients 13 with CS undergoing TAVI, 10% and 20% present significant left main CAD and proximal 14 left anterior descending artery stenosis, respectively.⁴¹ The coexistence of CAD and 15 16 secondary MR is much more frequent. More than two thirds of patients undergoing transcatheter edge-to-edge repair (TEER) have relevant CAD.⁴² Therefore, ICA is 17 18 mandatory to rule out CAD. The objectives of ICA are to 1) identify treatable CAD, 19 aggravating the CS; 2) perform myocardial revascularization when needed; 3) obtain safe 20 and adequate arterial access for percutaneous mechanical circulatory support (MCS). 21 Except for CS in AMI, in case of coexisting CAD requiring revascularization and 22 significant VHD, due to lack of RCT, time-sequence of events – placement of MCS,





1 revascularization and emergency balloon valvuloplasty/TAVI or TEER – depend on team

2 experience, patient clinical status and VHD (Table 1).

3 <u>Invasive right heart catheterization</u>. Alongside diagnosing pulmonary hypertension, it was

- 4 previously broadly used for haemodynamic monitoring and treatment adjustment.
- 5 However, several registries reported considerable complications related to its routine use
- 6 for treatment monitoring, and, despite conflicting registry-evidences^{43,44}, the only RCT
- 7 demonstrated no additional benefit compared to TTE.^{45,46} Therefore, right heart
- 8 catheterization is not recommended for daily monitoring. It can be useful, alone or in
- 9 combination with left catheterization, for decision making or in selected cases during the
- 10 peri-interventional phase in experienced hands (Table 1). Moreover, selective use of
- 11 pulmonary artery catheters can be considered to guide medical decision in CS, particularly
- 12 in patients considered for or supported by MCS.^{47,48}
- 13
- 14

15 THERAPEUTIC STRATEGIES: GENERAL CONCEPTS

Both 2021 ESC/EACTS Guidelines for VHD management⁹ and 2021 ESC Guidelines for
diagnosis and treatment of acute and chronic HF¹¹ contain few recommendations on VHD
management in CS. CS is time-sensitive with rapidly increasing mortality, which diagnosis
and management should start as early as possible. Early identification and treatment of
underlying cause, along with haemodynamic stabilization and management of organ
dysfunction, are key.

- 22
- 23 Medical treatment and ancillary procedures





1 After initial fluid challenge (if appropriate), pharmacological management of CS consists 2 of intravenous (I.V.) vasoactive agents to improve organ perfusion by increasing CO and blood pressure.^{11,54} Pharmacological agents selection is largely empirical, and they must be 3 used with caution, starting at low doses and up-titrating with close monitoring.^{19,54,55} 4 5 Norepinephrine is the vasopressor of choice, despite potentially harmful increase in stroke volume and transvalvular gradient in case of AS and increase LV afterload.¹¹ Accordingly, 6 7 medical stabilization is often difficult in presence of VHD and a rapid escalation to other 8 strategies (mechanical support and/or intervention) is strongly advisable. 9 Triggering factors must be recognized and treated immediately. In case of acute 10 coronary syndrome, urgent revascularization is required regardless of VHD. Nishino et al. 11 showed that shorter symptoms onset-to-reperfusion time was an independent predictor of early MR improvement in AMI.⁴⁹ Out of 51 patients from TAVI-SHOCK Registry, 33% 12 had CAD but only one (2%) presented AMI.⁵⁰ 13 14 Other causative factors include valve thrombosis especially within 12 months of prosthetic valve implantation, when it is the most common valve dysfunction cause.^{51,52} 15 16 Anticoagulation using VKA and/or UFH is the first-line treatment of biological valve 17 thrombosis. Fibrinolysis is an option (streptokinase was most commonly used fibrinolytic 18 agent, followed by t-PA and urokinase at standard recommended doses of each agent) in obstructive, especially mechanical, valve thrombosis, ⁵³. However, considering the risks of 19 20 bleeding, systemic embolism and recurrent thrombosis, emergency surgical valve 21 replacement is recommended over fibrinolysis if immediately available and not 22 contraindicated⁹.

23





1

2 Mechanical circulatory support devices

3 Evidence regarding outcomes of MCS in CS with VHD remains scarce, deriving mainly from small case series or registries, ^{50,56–60} and there are no published guidelines for short-4 5 term MCS in this setting. Hence, unselected use of MCS is not supported and requires 6 multidisciplinary expertise for device selection, implantation, and management. In 7 persisting severe haemodynamic deterioration and CS despite medical support and 8 triggering factor removal, early MCS could increase CO and end-organ perfusion, as a bridge-to-recovery, bridge-to-destination or bridge-to-bridge.^{11,19,47} Different temporary 9 10 MCS are currently available, including: intra-aortic balloon pump (IABP), veno-arterial 11 extracorporeal membrane oxygenation (VA-ECMO), the Impella (Abiomed Europe 12 GmbH, Aachen, Germany), the Tandem-Heart percutaneous system (Cardiac Assist, Inc, 13 Pittsburgh, PA, USA) and percutaneous LV assist devices. Device selection requires indepth understanding of anatomy, physiology, and pathology of VHD.^{19,47,48} 14 In severe AS, most MCS options may be used.⁴⁸ VA-ECMO may increase LV afterload 15 16 and, in some cases, concomitant LV unloading is mandatory, requiring unloading devices 17 such as a microaxial flow pump device if not contraindicated, or through atrial septostomy. 18 In MS, where LV end diastolic pressure is generally low, the optimal device would be 19 TandemHeart (with direct LA drainage). However, especially in RV failure and 20 hypoxemia, VA-ECMO would be best, with the preferred use of LA VA-ECMO modality. 21 In patients with CS due to AMI with papillary muscle rupture and acute MR, intra-aortic balloon pump (IABP) may be considered according to ESC guidelines^{11,61}, to decrease 22 23 afterload, supporting adequate mean arterial pressure and potentially decreasing MR,



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1 despite minimal CO augmentation. ECMO can better support CO, but is less commonly 2 used alone, since it may increase total peripheral vascular resistance, potentially worsening 3 MR. More frequently, in MR, physicians should consider LA VA-ECMO modality to 4 unload the LA or Impella device, alone or with ECMO (ie, ECPELLA), to directly unload the LV (caution needed in papillary muscle rupture-related MR).^{19,47,62} 5 6 Given AR pathophysiology, most (if not all) MCS are relatively contraindicated, especially in presence of concomitant aortic dissection.⁴⁸ In fact, elevated diastolic blood pressure 7 8 during IABP inflation, and increased afterload due to VA-ECMO, may both increase AR 9 and contribute to LV distention. Similarly, LVAD and Impella (precluding aortic valve 10 coaptation) may worsen AR and recirculation, reducing device' forward flow. If MCS is 11 absolutely necessary in severe AR, TandemHeart or LA VA-ECMO could be considered due to concomitant LA unloading.^{19,47,48} 12 13 MCS including ECMO, IABP, Impella® and TandemHeart have also been used in highrisk transcatheter valve procedures during CS.^{63–65} This use vary widely depending on 14 15 institutional practice and expertise but, it was demonstrated that a 'standardized team-16 based approach' with predefined algorithms for early MCS implant and close monitoring 17 of clinical signs, invasive haemodynamics and biochemical markers, may translate into improved survival.66-68 18 19

20 Valvular intervention

On top of pharmacological and organ-specific support, valvular intervention can be
 considered when VHD is the primary cause or an aggravating factor in CS (*Central*





| 1 | <u>Illustration</u>). Significant VHD is associated with increased in-hospital mortality in CS, ⁶⁹ |
|----|--|
| 2 | and early treatment is advocated because delay between CS onset and valvular intervention |
| 3 | predicted poor outcomes in patients with AS and CS. ^{41,70} Interestingly, in the IREMMI |
| 4 | registry, time between shock onset and TEER for acute MR was around 30 days. ⁷¹ Prior to |
| 5 | TEER, 66% of patients were stabilized with IABP or Impella® and 12% with VA-ECMO. |
| 6 | However, the authors advocated for early MR correction irrespective of LVEF and |
| 7 | development of CS. ⁷¹ |
| 8 | The Heart Team must decide the indication, timing and mode of intervention (surgical vs. |
| 9 | transcatheter), taking into account patients' clinical status and risk profile, anatomical |
| 10 | considerations (i.e., type of VHD, presence of combined VHD, aortic disease or CAD), |
| 11 | role of VHD in the CS, as well as institutional expertise and patients' values and |
| 12 | preferences. Contraindications for intervention in patients with CS, include: |
| 13 | 1. Severe frailty, limiting life expectancy (< 6-12 months), or refusal of life-saving |
| 14 | treatment. |
| 15 | 2. Non-severe VHD. |
| 16 | 3. End-stage CS with severe end organ failure (the "point of no return" was crossed). |
| 17 | 4. CS complicated by resuscitated cardiac arrest with unfortunate neurological |
| 18 | outcome. |
| 19 | 5. Possibility and indication for urgent heart transplantation with or without previous |
| 20 | MCS as bridge therapy (i.e., end-stage HF patients with functional MR). |
| 21 | Some of these contraindications are relative and dynamic; hence, patients should be closely |
| 22 | monitored and the decision adjusted according to the patient's clinical status. Regarding |





1 the mode of intervention (surgical vs transcatheter), very few data are available to support 2 either choice. Urgent/emergent cardiac surgery in VHD and CS is at high morbidity and mortality risk,^{72–74} and a less invasive approach with at least equal results might be 3 4 preferable. This can be more intuitive with TAVI, but less evident with other transcatheter 5 valve interventions. RCTs are needed to confirm this hypothesis, but hard to carry out in 6 this setting. Regardless of the strategy, acute correction of VHD in CS can potentially 7 reverse fatal process, allowing for recovery, and improving long-term patient outcomes. 8 Emergent or urgent surgical treatment of VHD leading to CS is advisable as a first-line 9 therapy (particularly in young patients and those with low comorbidity), or as the only 10 therapeutic option in some setting (i.e. active endocarditis or acute AR associated to type A 11 aortic dissection), if surgical risk allows it. Benefit of early surgery in infective 12 endocarditis is uncertain due to high recurrence rate, and its timing must be carefully 13 selected. Therefore, surgery in the acute setting is restricted to specific clinical situations 14 (HF, uncontrolled infection and prevention of embolic events) and eligible patients.⁷⁵ In 15 other cases, and in the absence of haemodynamic refractory instability, surgery is 16 postponed to allow 1 or 2 weeks of antibiotic treatment under careful clinical and echocardiographic observation.^{75,76} 17 18 Few surgical reports indicate that immediate surgical aortic valve replacement is feasible in

rew surgreat reports indicate that inintedate surgreat abrite valve replacement is reasone in
critically ill and decompensated patients with AS, with an in-hospital mortality of 2530%.^{77–79} In MR with CS, primary and secondary MR should be distinguished. In MR
caused by AMI, standard of care is acute surgical revascularization with simultaneous
mitral valve repair or replacement, despite high risk in CS (early mortality up to 2030%)⁸⁰. Peri-operative short-term MCS may be beneficial. In acute ischaemic MR, only



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| 1 | papillary muscle and chordal ruptures usually need immediate intervention. Accordingly, |
|----|--|
| 2 | of \approx 8% of patients with CS due to severe MR complicating AMI in the SHOCK Trial |
| 3 | Registry, only 46% underwent mitral valve surgery. ⁸¹ Surgery of papillary muscle rupture |
| 4 | carries higher mortality rate compared to regular mitral surgery owing to acute setting. ⁸¹ |
| 5 | As rapid deterioration after papillary muscle rupture is unpredictable, early intervention is |
| 6 | mandatory, even though intravenous diuretic and vasodilator/inotropic support may |
| 7 | initially stabilize patients. ⁸² |
| 8 | Emergency transcatheter valve treatments across different structural VHD complicated by |
| 9 | CS are described below, in dedicated sections. |
| 10 | In general, specific contraindications for transcatheter intervention include: |
| 11 | 1. Unfavourable valve or vascular anatomy; |
| 12 | 2. Percutaneous intervention not achievable (i.e., intra-chamber thrombus, valvular |
| 13 | thrombosis, mitral valve anatomy not suitable for TEER - same contraindications as |
| 14 | in stable patients). |
| 15 | 3. Active endocarditis (for transcatheter implantation of devices and valvular |
| 16 | replacement); |
| 17 | 4. Feasible and potentially more beneficial valvular surgery despite increased surgical |
| 18 | risk according to Heart Team consensus. |
| 19 | |
| 20 | URGENT/EMERGENT TRANSCATHETER VALVE TREATMENTS ACROSS |
| 21 | DIFFERENT VHD |
| 22 | Native AS and CS |





1 TAVI has a class I indication in symptomatic severe AS at high or prohibitive 2 surgical risk.⁹ CS represents a high-risk surgical condition, but RCTs of TAVI in this 3 setting is not available as CS was an exclusion criterion in most RCTs evaluating therapies 4 targeting both AS and HF. Therefore, current guidelines still recommend balloon aortic 5 valvuloplasty (BAV) in AS with decompensated HF and/or CS for stabilization as bridge to TAVI or surgical aortic valve replacement (Class IIb, level of evidence C).⁹ However, 6 7 despite initial success of urgent BAV, early mortality of these patients remains high (up to 71%).^{83–92} Recently, urgent/emergent TAVI has been suggested as an alternative when 8 available^{41,50,70,89,93,94} (Table 2). Theoretical advantages of TAVI over BAV in this setting 9 10 may be a better and sustained haemodynamic improvement with complete relief of 11 afterload mismatch and low residual AR risk, potentially translating into better outcomes and lower rates of early readmission.⁹⁶ Notwithstanding, TAVI may be more challenging 12 13 due to larger vascular access, higher vascular complications risk and the inconstant availability and feasibility of pre-procedural MSCT.⁸⁹ Moreover, urgent TAVI is not 14 15 feasible in all hospitals and transfer might be needed. Finally, even in hospitals with TAVI 16 availability, urgent TAVI may not be rapidly feasible for logistic reasons. (Table 3). Masha et al. reported the TAVI largest series in CS (4.1% of the U.S. TAVI population),⁴¹ 17 18 comparing 2,220 emergent TAVI for CS to 12,851 high-risk patients without CS (median 19 STS score 10.2) included in the STS/ACC TVT registry between 2014 and 2017. Despite 20 similar optimal gradient relief, CS population had higher complications rates and 30-day 21 mortality (19.1% vs. 4.9%), primarily driven by pre-procedural shock severity rather than 22 procedural complications. Impact of CS duration prior to treatment is well known, and 23 available evidence suggests that AS should be promptly corrected (BAV or TAVI) -





1 ideally within 48 hours from CS onset, as >48 hours delay was linked to worse 2 prognosis.^{86,89,90} However, ideal time window and accurate criteria for intervention remain unknown. Given procedural risks, it should be undertaken after Heart Team discussion in 3 4 experienced centres. Decision-making should consider feasibility, efficacy and utility of 5 emergent TAVI over other treatments, including medical management, BAV, durable LV 6 assist devices, and palliative care (Figure 3). There is no uniform definition of futility; however, in TAVI, it can be described as death and/or absence of functional improvement 7 6 to 12months post-procedure.⁹⁷ 8 9 Considerable knowledge gaps also exist regarding specific technical considerations, such 10 as 1) timing of coronary revascularization of concomitant CAD; 2) valve choice; 3) usefulness of intraprocedural MCS (i.e., "protected TAVI").^{98,99} Regarding valve choice, 11 12 there is no RCT and interventionalists should rather use the device they are most familiar 13 with. Furthermore, devices anticipating best outcomes with least hemodynamic 14 compromise during deployment should be preferred. 15 Bicuspid aortic valve disease. In the specific and not uncommon setting of bicuspid severe 16 AS, especially in the youth, cardiac surgery should be considered. BAV can be undertaken 17 in non-calcified valves with minimal AR (for example during pregnancy), as a bridge-to-18 surgery. In older patients with calcified valves, TAVI remains an option, provided accurate 19 valve evaluation, sizing and preprocedural planning by MSCT. 20 21 Native AR and CS

- 22 Given the high surgical risk, TAVI may be an alternative for pure (non-calcified) AR¹⁰⁰⁻¹⁰⁶
- also in CS, as reported in case reports or small series (Table 4).^{107–110} It is generally





1 contraindicated in endocarditis and aortic dissection. The Endo-Bentall procedure for 2 transcatheter treatment of acute aortic dissection complicated by acute AR is promising.¹¹¹ 3 Concerning AR in LV assist device patients, casuistics and meta-analyses demonstrate challenges and potentials of transcatheter treatment.^{109,112} 4 There is currently only one CE-marked device for pure AR.¹⁰⁰ Procedural challenges with 5 TAVI in pure AR include 1)lack of calcification for annulus visualization and valve 6 7 anchoring; 2)large annular size exceeding the manufacturer's recommendations for available transcatheter heart valves sizes. Future devices' iterations may overcome these 8 9 limitations.

10

11 Native MS and CS

12 PMBV in rheumatic MS has revolutionized the treatment of rheumatic MS since its

13 introduction in 1984.^{113,114} It is recommended for severe symptomatic MS without

14 unfavourable anatomic characteristics for mitral commissurotomy according to the 2021

15 ESC/EACTS Guidelines VHD management.⁹

This is particularly appealing in CS, as the procedure is less invasive than surgery and can be performed quickly, on an emergency basis, and under local anaesthesia. Several case reports described its use in this setting.^{115–118} In patients who are not good candidates for PMBV, transcatheter mitral valve implantation (TMVI) could offer a minimally invasive alternative, even though most techniques are much more challenging, require general anaesthesia and thorough pre-procedural planning. Besides, widespread availability and

22 longer-term follow-up is lacking.





1 In the specific case of pregnant women with severe HF, use of PMBV has been described 2 with substantial improvement in clinical outcomes and acceptable safety.¹¹⁹ Its yield in CS has been described in a case report.¹²⁰ Radiation exposure during PMBV carries a foetal 3 4 risk, especially during organogenesis. Every effort should be made to postpone the procedure to second trimester, after the fourth month, when organogenesis is complete and 5 thyroid is still inactive.¹²¹ However, when CS occurs, postponing the procedure may not be 6 7 possible. In this case, radiation doses should be kept as low as reasonably achievable 8 (ALARA) and dedicated protocols are warranted to minimize foetal radiation and iodine-9 based contrast medium due to the risk of neonatal hypothyroidism (Supplemental Table 2). 10

11 Native MR and CS

12 Postoperative outcome of emergency surgery (repair or replacement) for acute severe MR, 13 regardless of aetiology is poor with an overall 30-day mortality of 22.5%, even higher in AMI-related MR complicated by CS (up to 26.9%).¹²² Role of transcatheter interventions 14 15 in patients with MR and CS has not been fully demonstrated. There are no specific RCTs 16 completed to date (The "Transcatheter Mitral Valve Repair for Inotrope Dependent 17 Cardiogenic Shock (MINOS)" - NCT05298124 - is ongoing) and patients in CS were excluded from landmark trials of transcatheter mitral valve repair.^{123–125} However, several 18 case reports and recent observational studies described good results(Table 5).^{59,62,71,126–132} 19 20 Available evidence concerns almost exclusively one TEER device; use of TMVI in this 21 setting has not been reported. Of note, most data pertain to secondary, especially 22 ischaemic. MR.





1 Comparison among studies is limited by differences in population, methods and outcomes 2 assessment. Still, available evidence suggests that MitraClip® (Abbott Vascular, Abbott 3 Park, Illinois, USA) is associated with high procedural success (72.7-100%), and 4 acceptable short and mid-term outcomes (30-day or in-hospital mortality 0-27.3%, with a 5 single-center study reporting a 30-day mortality of 60%; 6-month or follow-up mortality 16.7-63.0%).^{59,62,71,126–132} In the largest study published to date, Jung et al. pooled data 6 7 from several observational studies, and performed a patient-level analysis of 141 patients 8 with CS and moderate to severe acute ischaemic MR; 78.7% of patients required inotropes 9 and about half were on MCS. Most had secondary MR (75.2%). Procedural success was 10 high (88.7%), with a relatively low overall mortality (in-hospital mortality 15.6%, 90-days mortality 29.5%, and one-year mortality 42.6%). Successful TEER was associated with 11 74% relative reduction in both in-hospital and 90-day mortality.¹²⁶ Tang et al. compared 12 13 the outcome of patients receiving MitraClip® during the index hospitalization to those who 14 did not using propensity-matched data from the Centers for Medicare and Medicaid 15 Services in the United States. They showed increasing device use throughout the study, 16 and significantly lower in-hospital (24.8% versus 35.4%; odds ratio 0.6; 95% confidence 17 interval (CI) 0.47-0-77; p<0.001) and one-year mortality (hazard ratio 0.76; 95% CI 0.65-18 0.88; p<0.001) in patients undergoing TEER. This benefit was consistent in all subgroups, except for patients requiring acute MCS or haemodialysis at the time of intervention.¹³³ 19 20 These preliminary results, even if encouraging, should be considered with caution. More 21 robust data should be obtained and the role of other techniques including TMVI must be





- assessed. In the meantime, TEER in CS should be considered in experienced hands and
 after careful feasibility evaluation.
- 3

4 **BVF and CS**

- 5 According to EAPCI consensus and VARC-3 definition,²⁰ BVF is defined by 1) clinically
- 6 expressive bioprosthetic valve dysfunction or irreversible severe HVD, 2) valve
- 7 reintervention, and 3) valve-related death.^{134–136}

8 Transcatheter treatment for Stage 3 HVD and CS depends on underlying pathology and

- 9 time from index procedure.
- 10 <u>Short interval (<12 months):</u> Valve thrombosis is the most common cause of

11 dysfunction.^{51,52} Its treatment has previously been described (see *Medical treatment and*

- 12 *ancillary procedures*). New valve regurgitation is related to valve migration, PVL, or
- 13 endocarditis.¹³⁷ Plug implantation is gold-standard for non-surgical patients with PVL.^{138–}

14 ¹⁴⁰ Valve-in-valve can restore valve function and haemodynamics in unstable patients with

15 migrated transcatheter or sutureless valves, and inoperable patients with subacute

- 16 endocarditis.^{141,142}
- 17 <u>Long interval (>12 months)</u>: Most common causes are degeneration and endocarditis, even
- 18 if endocarditis decreases one year after valve implantation (approximately 1% per person-
- 19 year vs 0.5% per person-year afterwards).¹⁴³ In case of valve-in-valve, characteristics of
- 20 the bioprosthesis should be taken into account (Table 6). CS context would require fast and
- 21 effective transcatheter procedure. However, some anatomical conditions like small internal
- 22 diameter of degenerated bioprosthesis and high coronary obstruction risk, or outflow tract
- 23 obstruction risks, will require sophisticated techniques to achieve optimal procedural





- outcome^{145,146} (Table 7). Those situations will require general anaesthesia to allow TEE
 guidance, and potentially MCS to stabilize haemodynamics during longer procedures.
- 3

4 CONCLUSIONS

5 CS is a clinical condition of extremely high morbidity and mortality where severe VHD is associated with increased mortality.⁶⁹ Acute onset of severe VHD may be the cause of CS, 6 7 or triggering factors acting on pre-existing stable severe VHD can cause CS. In both 8 situations, pharmacological support is the first line therapy, including removal and 9 treatment of triggering factors. However, if haemodynamic status is not quickly reverted, 10 rapid escalation to other non-pharmacological treatment, particularly correction of 11 concomitant VHD, may be required. Treatment decision should consider procedural utility 12 and futility. Given the extremely high mortality risk, less invasive transcatheter valve 13 interventions can be used as an alternative to surgery in several situations. Heart Teams 14 must guide decision-making regarding indications, timing and mode of intervention, 15 according to patients' clinical status and risk profile, anatomical considerations, VHD role, 16 institutional expertise, and patients' values and preferences. As outlined above, to date, 17 most evidence stems from case series and registries. The very high mortality risk warrants 18 dedicated, well-designed and adequately powered RCTs to further elucidate the role of 19 transcatheter valvular interventions and could, if positive, have significant public health 20 implications. While CS RCTs are complicated by time pressures and patients' heterogeneity, clear inclusion criteria render such trials feasible and effective.¹⁴⁷ We 21 22 believe that in the meantime, all CS patients, if not eligible for ongoing RCTs, should be 23 included in registries embedded in network of networks, or a hub-and-spoke registry, that





1 will allow high-quality retrospective analyses in large, worldwide dataset, and may assist

2 in future registry-based RCTs.¹⁴⁸

- 3
- 4 FUNDING STATEMENT: This research received no specific grant from any funding
- 5 agency in the public, commercial or not-for-profit sectors.
- 6
- 7 CONFLICT OF INTEREST:

Nikolaos Bonaros reports grants from Edwards Lifesciences and Corcym and lecture fees 8 9 from Edwards Lifesciences and Medtronic. Pedro Carrilho-Ferreira reports lecture fees 10 from Astra Zeneca, A. Menarini, Bayer, Biotronik, Medinfar, Medtronic and Advisory Board for Medtronic. Martin Czerny is Consultant for Terumo Aortic, Medtronic, 11 Endospan and NEOS and Shareholder TEVAR Ltd and Ascense Medical. Chiara Fraccaro 12 13 reports Support for attending meetings from Medtronic. Christian Hassager reports Research grants from Novo Nordisk Foundation and Lundbeck Foundation and Lecture 14 15 honorarium from Abiomed. Nicole Karam reports consulting and lecture fees from Medtronic, Edwards and Abbott Vascular. Won-Keun Kim reports lecture fees and 16 honoraria from Abbott, Boston, Meril, Edwards, Medtronic, Shockwave. Konstantin A. 17 Krychtiuk reports lecture and/or consulting fees from Amgen, Novartis, Sanofi. Helge 18 19 Möllmann received speaker honraria/proctor fees from Abbott, Boston Scientific, Edwards 20 Lifesciences, Medtronic. Jerzy Pregowski reports lecture fees from Abbott and Edwards 21 and contracts from Abbott. Giuseppe Tarantini reports lecture fees from Medtronic, Edwards Lifesciences, Abbott Vascular, Boston Scientific, GADA, Abiomed. Julien 22 23 Ternacle reports consulting fees from Abbott, General Electric and Philips Healthcare and lecture fees from Edwards. All other authors have nothing to disclose. 24

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1 Figure legends

2 Central Illustration. Diagnostic and therapeutic algorithm in cardiogenic shock and

- 3 valvular heart disease.
- 4 Diagnostic and therapeutic algorithm leading to valve intervention when a valve heart
- 5 disease is either the primary cause or an aggravating factor in cardiogenic shock. *The
- 6 mentioned valve disorders are the most common examples.
- 7 *PVL=paravalvular leak; TAVI=transcatheter aortic valve implantation;*
- 8 *TEER=transcatheter edge-to-edge repair; VHD=valvular heart disease*
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10 Figure 1. Identification of BVF mechanisms associated with cardiogenic shock.

- 11 BV: bioprosthetic valve, HALT: hypoattenuated leaflet thickening, HVD: haemodynamic
- 12 valve deterioration, MSCT: multislice computed tomography, RLM: reduced leaflet
- 13 *motion, TEE: transoesophageal echocardiography, TTE: transthoracic echocardiography.*
- 14 ** for HVD severity definition.*
- 15 * Stage 1 HVD definition: Evidence of SVD, non-structural valve dysfunction (other than
- 16 paravalvular regurgitation or prosthesis-patient mismatch), thrombosis, or endocarditis
- 17 without significant haemodynamic changes.
- 18 * Stage 2 HVD definition: Increase in mean transvalvular gradient ≥ 10 mmHg resulting in
- 19 mean gradient \geq 20 mmHg with concomitant decrease in EOA \geq 0.3 cm2 or \geq 25% and/or
- 20 *decrease in Doppler velocity index* ≥ 0.1 *or* $\geq 20\%$ *compared with echocardiographic*
- 21 assessment performed 1–3 months post-procedure, OR new occurrence or increase of ≥ 1
- 22 grade of intraprosthetic AR resulting in \geq moderate AR.





* Stage 3 HVD definition: Increase in mean transvalvular gradient ≥20 mmHg resulting in
mean gradient ≥30 mmHg with concomitant decrease in EOA ≥0.6 cm2 or ≥50% and/or
decrease in Doppler velocity index ≥0.2 or ≥40% compared with echocardiographic
assessment performed 1–3 months post-procedure, OR new occurrence, or increase of ≥2
grades of intraprosthetic AR resulting in severe AR.²¹

6

Figure 2. Proposed diagnostic workflow for the assessment of patients presenting with CS.

Step 1. Point-of-care cardiac ultrasound. Point-of care cardiac ultrasound is generally 9 useful as it provides the first clues for a severe VHD.¹⁴⁹ However, it is rarely sufficient. In 10 11 this phase, ruling out acute myocardial ischemia, advanced cardiomyopathies, intolerated 12 arrhythmias, acute pulmonary embolism, tamponade or type A acute aortic dissection potentially responsible for the CS, is crucial.¹⁵⁰ When point-of-care cardiac ultrasound 13 14 reveals hyperdynamic LV function in a patient with severe acute decompensated heart 15 failure or CS, urgent assessment with comprehensive transthoracic echocardiography 16 (TTE) is warranted to exclude VHD emergencies. 17 Step 2. Comprehensive TTE. Comprehensive TTE is generally adequate to accurately 18 investigate valve structure and function. Importantly, increased flow due to sepsis or 19 anaemia can elevate Doppler gradients, potentially leading to overestimation of the 20 severity of stenotic valve lesions. Likewise, volume overload and systemic hypertension 21 often lead to reversible worsening of regurgitant lesion severity. Conversely, low flow 22 status might underestimate the severity of valvular diseases. Invasive coronary





1 angiography +/- invasive haemodynamic assessment can give in this step additional 2 information. At this step, an invasive coronary angiography is indicated to rule out concomitant CAD according to guidelines criteria⁹. Alternatively, owing to its high 3 4 negative predictive value, MSCT may be used in patients who are at low risk of 5 atherosclerosis. 6 Step 3. Complementary valve-specific diagnostic tools include TEE and/or Multislice 7 Computed Tomography. Accurate quantification of VHD severity is essential, as only severe valvular dysfunction can cause CS.¹⁵¹ Hence, TEE, including 3D modalities, is 8 9 useful in the detailed assessment of valve anatomy and function (native or 10 prosthetic)¹⁵²and should be systematically performed when TTE is inconclusive. In 11 stabilized patients, MSCT should be performed if required for the planification of the 12 transcatheter heart valve intervention. 13 Figure 3. Factors influencing utility versus futility of emergent TAVI in case of 14 15 patients with AS and CS. 16 17 18 19 20





1 Table 1. Checklist for VHD imaging assessment and eligibility to transcatheter

2 procedures.

| | | FOR DIAGNOSIS | FOR ELIGIBILITY TO TRANSCATHETER PROCEDURES |
|------------|-------|---|--|
| | TTE | Confirm AV disease severity Evaluate valve morphology Check for associated VHD, LV/RV function, PASP | |
| | TEE | Confirm diagnosis (optional) | Confirm annular sizing (3D evaluation, only if MSCT not available) |
| AV disease | MSCT | Confirm VHD severity (calcium score) in LFLG AS Rule out CAD in selected cases | Confirm annular sizing Evaluate valve morphology and calcium distribution General aortic root assessment (Sinus of Valsalva and STJ dimension, coronary ostia height) Evaluate aorta and vascular access |
| | ICA | Rule out CAD | |
| | L-RHC | Confirm disease severity in selected cases | |
| | TTE | Confirm MV disease severity Evaluate valve morphology and mechanism of VHD Check for associated VHD, LV/RV function, PASP | |
| MV disease | TEE | Confirm diagnosis in selected cases | Evaluate valve morphology and mechanism of MR for TEER and TMVI Rule out LAA and LA clots |
| | MSCT | Rule out CAD in selected cases | Evaluate annulus size for TMVI eligibility Predict LVOT obstruction for TMVI eligibility |
| | ICA | Rule out CAD | |
| | L-RHC | Confirm disease severity in selected cases | |
| | TTE | Confirm BVF severity Evaluate valve morphology and mechanism of failure Check for associated VHD, LV/RV function, PASP | |
| | TEE | Confirm mechanism of bioprosthetic valve dysfunction (SVD, non-SVD, thrombosis, endocarditis) Discriminate between PVL and intra-valvular AR | Rule out LAA and LA clots in case of planned valve-in-valve in mitral position Identify PVL location to select the most appropriate vascular access for transcatheter occlusion |
| BVF | | | Confirm valve size Identify PVL location to select the most appropriate vascular access for transcatheter occlusion Evaluate vascular access |
| | MSCT | Confirm mechanism of bioprosthetic valve dysfunction (SVD, non-SVD, thrombosis, endocarditis) Rule out CAD in selected cases | + IN AORTIC POSITION: General aortic root assessment (Sinus of Valsalva and STJ dimension, coronary ostia height) Check for interference with coronary ostia Evaluate aorta and vascular access |
| | | | + IN MITRAL POSITION: Predict LVOT obstruction |
| | ICA | Rule out CAD | |
| | L-RHC | Confirm disease severity in selected cases | |



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| 1 2 3 4 5 6 7 8 9 10 | AR=aortic regurgitation; AS=aortic stenosis; AV=aortic valve; CAD=coronary artery disease; ICA=invasive coronary angiography; L-RHC=left-right heart catheterization; LA=left atrial; LAA=left atrial appendage; LFLG=low flow low gradient; LV=left ventricular; LVOT=left ventricular outflow tract; MSCT=multislice computed tomography; MV=mitral valve; PASP=pulmonary artery systolic pressure; PVL=paravalvular leak; RV=right ventricular; STJ=sino-tubular junction; SVD=structural valve deterioration; TEE=transesophageal echocardiography; TTE=transthoracic echocardiography; TEER=transcatheter edge-to-edge repair; TMVI=transcatheter mitral valve implantation; VHD=valvular heart disease. |
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Table 2. Summary of registries on BAV and TAVI in CS.

| Author Setting | | Population Age, years | | LVEF, % | 30-day mortality | | | |
|-------------------------------------|-------------|--------------------------------|-----------------|-------------|-----------------------|--|--|--|
| BAV in patients with CS | | | | | | | | |
| NHLBI, 1991 ⁸³ | Multicentre | 39 BAV | - | - | 51% | | | |
| Cribier, 1992 ⁸⁴ | Monocentric | 10 BAV | 64 ± 9 (54-79) | 25±6 | 20% | | | |
| Moreno, 1994 ⁸⁵ | Monocentric | 21 BAV | 74 ± 3 (35-90) | 29 ± 3 | 43% (In- hospital) | | | |
| Buchwald, 2001 ⁸⁶ | Monocentric | 14 BAV | 74 ± 11 (50-91) | - | 71% | | | |
| Saia, 2013 ⁸⁷ | Monocentric | 23 BAV | 70 ± 13 | 40 ± 15 | 56.5% | | | |
| Theiss, 2014 ⁸⁸ | Monocentric | 13 BAV | 79 ± 2 | 33 ± 3 | 38.5% | | | |
| Bongiovanni, 2017 ⁸⁹ | Multicentre | 118 BAV | 81 ± 8 | - | 33.0% | | | |
| Debry, 2018 ⁹⁰ | Multicentre | 44 BAV | 77 ± 8 | 30 ± 14 | 47% | | | |
| Eugène, 201891 | Monocentric | 17 BAV | 79 ± 9 | 27 ± 11 | 48% | | | |
| Varela, 201992 | Monocentric | 14 BAV | 76 ± 7 | - | 21.4% | | | |
| | | TAVI in patients with | h CS | | | | | |
| D'Ancona, 2012 93 | Monocentric | 21 TAVI TA | 75 ± 11 | 26 ± 13 | 19% | | | |
| Frerker, 2016 ⁷⁰ | Monocentric | 27 TAVI | 78 ± 9 | 40 ± 15 | 33.3% | | | |
| Bongiovanni, 2017 ⁸⁹ | Multicentre | 23 TAVI | 76 ± 11 | - | 23.8% | | | |
| Fraccaro, 2019 ⁵⁰ | Multicentre | 51 TAVI | 76 ± 13 (31-93) | 43 ± 15 | 11.8% | | | |
| Huang, 2019 ⁹⁴ | Monocentric | 31 emergent TAVI (26/31 in CS) | 73 ± 14 | 32 ± 15 | 19.4% | | | |
| Masha, 2020 ⁴¹ | Multicentre | 2,220 TAVI | 83 (median) | 53 (median) | 19.1% | | | |
| Steffen, 2022 ⁹⁵ | Monocentric | 47 TAVI | - | - | 42.6% (@90- day) | | | |

BAV=balloon aortic valvuloplasty; CS=cardiogenic shock; LVEF=left ventricular ejection fraction; TA=transapical; TAVI=transcatheter aortic valve implantation.

5 6

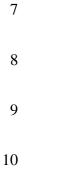






Table 3. Pro and cons of BAV and TAVI in CS. 1

| | | BAV | TAVI |
|--------|---|-------------------------|------------------------|
| | Residual transvalvular gradient | $\uparrow \uparrow$ | $\downarrow\downarrow$ |
| | Risk of significant post-procedural AR | $\uparrow\uparrow$ | \downarrow |
| | Insertion profile | \rightarrow | ↑ • |
| | Availability | $\uparrow\uparrow$ | ↑↓* ▲ ** |
| | Feasibility | $\uparrow\uparrow$ | ↑↓** ^^ |
| 2 | Costs *(potential need for transfer); **(need for | $\downarrow \downarrow$ | $\uparrow\uparrow$ |
| Z | (potential need for transfer); (need for | emergent CT scan) | |
| 3 | BAV=balloon aortic valvuloplasty; CS=cardioge | nic shock; TAVI=transca | theter aortic valve |
| 4 5 | implantation. | | |
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1 Table 4. Summary of studies (single case reports) on emergent TAVI for the

2 treatment of acute AR during CS.

| Author | Setting | Treatment | |
|-----------------------------------|--|------------------------------|--|
| Spina, 2019 ¹⁰⁷ | Acute AR after iatrogenic surgical injury during | Transfemoral TAVI (Medtronic | |
| | complicated mitral valve surgery | Evolut R) | |
| Herrmann, | Acute AR after iatrogenic injury from Impella® | Transfemoral TAVI (Edwards | |
| 2017 ¹⁰⁸ | implantation | Sapien 3) | |
| Van der Werf, | Acute AR in a left ventricular assist device | Transfemoral TAVI (Medtronic | |
| 2017 ¹⁰⁹ | patient | CoreValve) | |
| Abdelaziz, | Acute AR and aortic root dissection after | Transapical TAVI (Edwards | |
| 2018 ¹¹⁰ | previous supracoronary aortic replacement | Sapien S3) | |

| 4 5 | AR=aortic regurgitation; CS=cardiogenic shock; TAVI=transcatheter aortic valve implantation. |
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1 Table 5. Observational studies of transcatheter mitral valve repair in patients with

2 MR and CS*.

| Author | Settin g | n | Clinical scenario | Device | Mechanical circulatory support | Proce dural succes s | Outcomes |
|--|-----------------------|---------|---|---------------|--|-------------------------------|---|
| Adamo, 2017 ¹²⁷ | Single - centre | 4 | Secondary MR: 100% (acute MR post-AMI 100%) | MitraCli p | IABP: 100% | 100% | 30-day mortality: 0% |
| Seizer, 2017 ¹²⁸ | Single - centre | 10 | N/A | MitraCli p | IABP: 30.0% ECMO: 70.0% Impella: 30.0% | 90.0% | 30-day mortality: 60.0% |
| Flint, 2019 ¹²⁹ | Single - centre | 12 | Primary MR: 33.3% Secondary MR: 16.7% Mixed MR: 50.0% | MitraCli p | IABP: 33.3% ECMO: 8.3% | 75.0% | 30-day mortality: 16.7% Follow-up mortality (median 198 days): 41.7% |
| Chan, 2019 ¹³⁰ | Single - centre | 27 | Primary MR: 7.4% Secondary MR: 92.6% (ischaemic 92.0%) | MitraCli p | IABP: 18.5% | 92.6% | 30-day mortality: 25.9% Follow-up mortality (mean 202 days): 63.0% |
| Cheng, 2019 ⁵⁹ | Single - centre | 29 | Secondary MR: 100% (non- ischaemic 65.5%, ischaemic 34.5%) | MitraCli p | Impella: 17.2% IABP: 10.3% | 96.6% | In-hospital mortality: 17.2% Survival to 6 months: 75.6 ± 8.0% |
| Garcia, 2020 ¹³¹ | Single - centre | 11 | Primary MR: 63.6% Secondary MR: 36.4% | MitraCli p | IABP: 45.5% | 72.7% | 30-day mortality: 27.3% One-year mortality: 66.7% |
| Jung, 2021 ¹²⁶ | Multic entre | 14 1 | Primary MR: 23.4% Secondary MR: 75.2% Mixed MR: 1.4% | MitraCli p | 50.4% | 88.7% | In-hospital mortality: 15.6% One-year mortality: 42.6% |
| Estévez- Loureiro , 2021 ⁷¹ | Multic entre | 50 | Secondary MR: 100% (acute MR post-AMI 100%) | MitraCli p | IABP/Impella: 66.0% VA ECMO: 12.0% | 90.0% | 30-day mortality: 10.0% Follow-up mortality (median 7 months): 28% |
| Vanden briele, 2021 ⁶² | 2 centre s | 6 | Primary MR: 50% Secondary MR: 50% | MitraCli p | Impella: 100% | 100% | In-hospital mortality: 16.7% 6-month mortality: 16.7% |





| Falasco ni, 2021 ¹³² | Multic entre | 31 | Secondary MR: 100% (papillary muscle rupture 12.9%) | MitraCli p | IABP: 58.1% Impella: 22.6% ECMO: 6.5% | 87.1% | 30-day mortality: 22.6%6-month mortality:38.7% |
|---------------------------------------|-----------------|----|--|---------------|---|-------|--|
|---------------------------------------|-----------------|----|--|---------------|---|-------|--|

| 1 | |
|----------|---|
| 2 3 | ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; AMI: myocardial infarction; MR: mitral regurgitation; N/A: not available; VA: veno-arterial |
| 4 5 | * Studies including exclusively patients with cardiogenic shock or studies including also patients without cardiogenic shock, but in which data on patients with cardiogenic shock could be extracted from the manuscript |
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1 Table 6. Transcatheter treatment options in case of BVF.

| | | No/mild calcifications | Severe calcification |
|--------|-------------------|---|-----------------------------------|
| | Stenosis | Valve-in-valve | Valve-in-valve (consider cerebral |
| | | | protection) ¹⁴⁴ |
| | Regurgitation | Valve-in-valve | Valve-in-valve (consider cerebral |
| 2 | | Plug in case of severe PVL ^{138–140} | protection) ¹⁴⁴ |
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| 3 4 | B V F=bioprostnet | ic valve failure; PVL=paravalvular lea | К. |
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1 Table 7. Advanced techniques to overcome complex situations for valve-in-valve.

| Complex situations for valve-in-valve | Advanced techniques |
|--|--|
| Small aortic bioprosthesis (label size ≤ 21 | Bioprosthesis valve ring fracture |
| mm) | |
| Risk of coronary obstruction | Coronary chimney stenting, endovascular |
| | electrosurgery leaflet splitting ¹⁴⁵ |
| Risk of LV outflow tract obstruction in mitral | Endovascular electrosurgery leaflet |
| valve-in-valve | splitting ¹⁴⁶ , alcohol septal ablation |

LV=left ventricle



