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ORIGINAL PAPER

Prophylactic ECMO during TAVI in patients with depressed left ventricular ejection fraction

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Abstract

Background This study investigated the impact of prophylactic veno-arterial extracorporeal membrane oxygenation (pECMO) in patients with depressed left ventricular ejection fraction (dLVEF) undergoing transcatheter aortic valve implantation (TAVI).

Methods Out of 1490 patients undergoing TAVI at two centers (2010–2015), 222 patients had dLVEF (≤40%). Of these, 21 patients (10%) underwent TAVI with pECMO. Complications and outcome according to pECMO were analyzed in the entire and in a propensity-matched population.

Results In the entire population, patients with pECMO had a higher logEuroScore I (33% ± 19 vs. 25% ± 17; $p=0.037$), worse LVEF (26% ± 7 vs. 32% ± 7; $p=0.001$), more major bleedings (29% vs. 9%; $p=0.015$), higher transfusion rate (30% vs. 10%; $p=0.019$) and longer in-hospital stay (9.0 [7.0;14.0] vs. 7.0 [5.0;10.0] days; $p=0.024$). After propensity matching only transfusion rate remained higher with pECMO (30% vs. 7%; $p=0.025$). In the entire population, rate and risk of 30-day mortality was higher with pECMO (24% vs. 6%, HR 95%CI 4.29 [1.51–12.19]; $p=0.006$). In the matched population, this effect was attenuated (24% vs. 12%, HR 95%CI 2.09 [0.61–7.23]; $p=0.243$). Cumulative rate and risk of 1-year mortality did not differ in the entire (log-rank $p=0.069$; 39% vs. 22%, HR 95%CI 1.99 [0.94–4.24]; $p=0.074$) nor in the matched population (log-rank $p=0.520$; 39% vs. 31%, HR 95%CI 1.34 [0.55–3.28]; $p=0.523$).

Conclusion In patients with dLVEF undergoing TAVI, periprocedural pECMO support does not seem to improve patient outcome.

Keywords Depressed left ventricular function · Aortic stenosis · TAVI · ECMO · Multidisciplinary Heart Team

Introduction

Transcatheter aortic valve implantation (TAVI) is the treatment of choice for patients with symptomatic severe aortic stenosis with elevated surgical risk [1]. Patients with severe aortic stenosis and depressed left ventricular ejection fraction (dLVEF) constitute a high-risk subpopulation. Previous studies have shown that these patients have a poor prognosis with medical treatment and increased mortality when undergoing surgical aortic valve implantation or TAVI [2–6].

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Furthermore, dLVEF has been identified as an independent predictor of early mortality after TAVI [7]. Whether this reflects the natural course of the disease with poorer recovery from the procedure or is the result of a higher rate of procedural complications is unknown.

Elective or prophylactic veno-arterial extracorporeal membrane oxygenation (pECMO) may be a feasible procedural adjunct in patients who present with high perioperative risk to guarantee full hemodynamic capability during TAVI, as mandated by current guidelines [8]. Experience with prophylactic short-term hemodynamic support during high-risk TAVI procedures is limited. Data published so far suggest favorable clinical outcome in terms of survival, especially when considering the elevated risk profile of these patients [9–11]. However, the available data are limited due to small sample sizes and therefore the influence on outcome remains unclear.

In the present study, we analyzed the impact of pECMO during TAVI in patients with dLVEF from two high volume centers. To account for an inherent selection bias, all analyses were also conducted in a propensity-matched population.

Materials and methods

Patients and indications

From July 2010 to May 2015, 1,490 patients underwent TAVI for severe aortic stenosis, at the University of Regensburg Medical Center ($n = 817$) and the Department of Cardiology at the German Heart Center Munich, Technical University Munich ($n = 673$). Of these, 222 patients displayed a dLVEF ($\leq 40\%$) and formed the study population (Fig. 1).

Both centers are high-volume ECMO centers [12] and have a considerable experience in ECMO support with a yearly average of 90 and 60 vaECMO runs at the University of Regensburg Medical Center and German Heart Center Munich, respectively. The indication for pECMO was left to the discretion of the senior physicians performing the procedure, depending on the perceived pre-operative clinical and individual risk of the patient. Patients with dLVEF were retrospectively divided into two groups with either pECMO support or without pECMO. All cases were discussed in an interdisciplinary heart team and consensus was reached regarding the therapeutic strategy in each case. Written informed consent for the procedures was obtained from all subjects. Ethical approval for data collection was obtained at each participating side and the study was conducted in accordance to the Declaration of Helsinki.

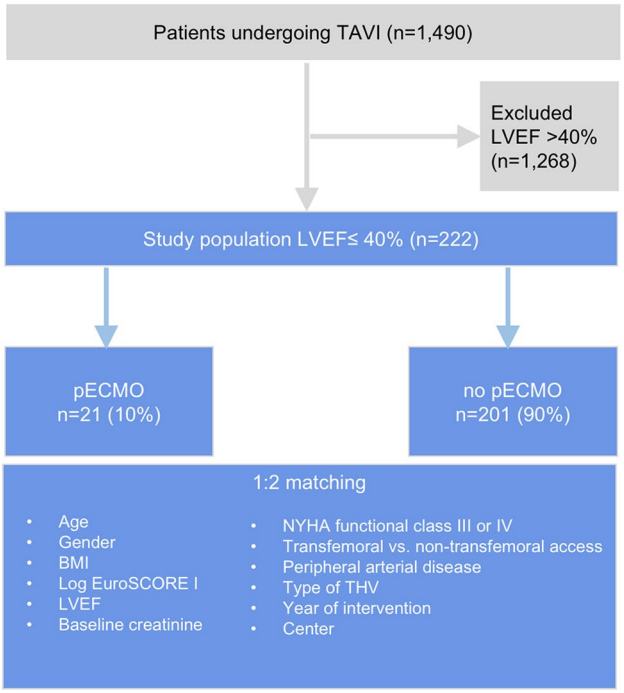

Fig. 1 Study population and variables used for propensity matching. *TAVI* transcatheter aortic valve implantation, *LVEF* left ventricular ejection fraction; *pECMO* prophylactic extracorporeal membrane oxygenation; *BMI* body mass index; *NYHA* New York Heart Association; *THV* transcatheter heart valve

Description of the procedures

TAVI was performed either via the transfemoral ($n = 161$) or transapical ($n = 60$) approach. In one patient ($n = 1$), an alternative transaortic access was chosen. For the transfemoral approach, the balloon-expandable valves SAPIEN XT™ (Edwards Lifesciences, Irvine, CA, USA) and SAPIEN 3™ (Edwards Lifesciences, Irvine, CA, USA) or the self-expandable prosthesis CoreValve™ (Medtronic, Irvine, CA, USA), Acurate NEO (Symetis SA, Eclubens, CH, USA), and Direct Flow Medical® (Direct Flow Medical Inc, Santa Rosa, CA, USA) were employed. For the transapical approach, the balloon-expandable SAPIEN XT™ (Edwards Lifesciences, Irvine, CA, USA) or the self-expandable prosthesis Acurate TA™ (Symetis SA, Eclubens, CH, USA) or Engager™ (Medtronic, Irvine, CA, USA) were used. All TAVI procedures were performed in the catheterization laboratory or hybrid-operating suite under general anesthesia or conscious sedation.

pECMO was initiated in the operating theater prior to TAVI using a femoral access in all cases. Details of pECMO implantation have been described previously [11, 13]. Briefly, a percutaneous pre-closure device (ProStar XL® or Perclose ProGlide®, Abbott Laboratories, Abbott Park) was put in place for arterial postprocedural

haemostasis. Arterial and venous cannulae (MAQUET AG, Hechingen, Germany) were selected according to patient's biometric data. An additional arterial access for angiographic catheters was employed with a Y-shaped side port. The veno-arterial ECMO circuit was initiated using a miniaturized pump (CardioHelp or ELS, MAQUET, Hechingen, Germany) as previously described [11, 14]. The flow rates and gas supply were adapted to achieve an adequate vasopressor-free circulation with a minimum of 500 ml/min and a target arterial oxygen partial pressure of 150 mmHg and normocapnia. During balloon valvuloplasty and deployment of the transcatheter heart valve, the pump was halted to avoid prosthesis dislocation.

Follow-up and definition of complications and endpoints

Follow-up data were prospectively collected in both centers during routine ambulatory visits at the outpatients' department or contacting the treating physician or other hospital documentation.

The primary endpoint was all-cause mortality during the first year after TAVI. Event-free patients were censored at one year or, in case of loss to follow-up at last contact alive (7/222, 3%). Follow-up was complete for all pECMO patients.

Outcomes and complications were analyzed and categorized according to the updated Valve Academic Research Consortium criteria (VARC-2) [15]. Procedural complications were further classified into ECMO related and non-related complications depending on the vascular site and type of complication.

Statistical analysis

Continuous variables are displayed as mean ± standard deviation or median [interquartile range] and analyzed using the unpaired Student *t* or Mann–Whitney *U* test. For comparison of group percentages, the Chi-square or Fisher's exact test were used. Missing baseline data (0.6%) were imputed using the predictive mean matching function (R-package "mice").

30-day and 1-year mortality rates were calculated as Kaplan–Meier estimates with the corresponding 95% confidence interval (CI). Cumulative mortality during 1 year after TAVI was visualized using the Kaplan–Meier method with differences tested using the log-rank test. The association of pECMO with time to 30-day and 1-year mortality was assessed using unadjusted and multivariate adjusted Cox proportional hazard regression analyses. The multivariable model was adjusted for covariates with a p value < 0.1 in the univariate analysis for 1-year mortality (age, logistic EuroScore I, elevated NYHA class (III/IV), access (transfemoral vs. non-transfemoral, THV type) (Supplemental Table 1). The hazard ratios (HR) with their 95% CI were computed.

To reduce imbalance in baseline characteristics and the effect of a potential selection bias for pECMO two approaches were applied. The multivariate model was repeated using inverse probability of treatment weighting using a propensity score to undergo TAVI with pECMO [16]. This propensity score was derived using binary logistic regression analysis. Variables for adjustment were selected based on their p value in the univariate analysis and on their potential influence on treatment allocation. The selected variables were: age, gender, BMI, logistic EuroScore I, NYHA class (III/IV), center, LVEF, creatinine, access, peripheral artery disease, THV type and year of treatment.

Finally, a matched population was created using the R-package "MatchIt". In short, 1–2 nearest neighbor matching was used to identify two control cases ($n = 42$) for each case treated with pECMO ($n = 21$). 1–2 matching was chosen to minimize play of chance in the control group, and thus to increase statistical power among controls. Variables used for propensity matching are displayed in Fig. 1. A two-sided p value < 0.05 was considered statistically significant. All analyses were performed using R (Version 3.3.2, R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics of the entire and matched population

Overall, 222 patients with dLVEF underwent TAVI. Of these, 21 patients underwent TAVI with pECMO for hemodynamic support during the procedure (10%, 21/222). Baseline characteristics of the entire study population are displayed in Table 1. Comparison of patients with and without pECMO showed a significantly higher logistic EuroScore I (33%±19 vs. 25%±17; $p = 0.037$) and a worse left ventricular ejection fraction (26%±7 vs. 32%±7; $p = 0.001$). In the group with pECMO, more patients were on renal replacement therapy (14%, 3/21 vs. 1%, 2/201; $p = 0.007$). After propensity matching for variables summarized in Fig. 1, there were no unmatched treatment units, leaving 21 patients with pECMO and 42 matched control cases undergoing TAVI without pECMO (Supplemental Fig. 1). Comparison after propensity matching showed no differences in baseline characteristics (Table 1).

Prophylactic ECMO characteristics and ECMO-related complications

pECMO was performed via femoral access in all cases and details on pECMO cannulation are shown in Table 2. Decannulation of the pECMO system was performed in all cases at the end of the procedure in the catheterization laboratory

Table 1 Baseline characteristics of the study population

	pECMO+, $n=21$	Entire population		Matched population	
		pECMO−, $n=201$	p value	pECMO−, $n=42$	p value
Clinical characteristics					
Age (years)	78.8 ± 6.8	80.0 ± 5.9	0.440	79.0 ± 7.3	0.898
Female gender	5 (23.8)	74 (36.8)	0.345	10 (23.8)	1.000
Body mass index (kg/m^2)	28.1 ± 6.1	26.3 ± 3.9	0.196	27.3 ± 3.9	0.582
Logistic EuroScore I (%)	33.2 ± 18.7	24.9 ± 17.0	0.037	29.6 ± 21.8	0.507
Hypertension	17 (81.0)	165 (82.1)	0.999	36 (85.7)	0.719
Hypercholesterolemia	8 (38.1)	100 (49.8)	0.431	20 (47.6)	0.654
Diabetes mellitus	11 (52.4)	69 (34.3)	0.161	16 (38.1)	0.418
Ever smoker	4 (19.0)	39 (19.4)	0.999	10 (23.8)	0.757
Creatinine (mg/dl)	1.6 ± 0.8	1.3 ± 0.7	0.122	1.5 ± 0.8	0.818
NYHA III/IV	21 (100)	174 (86.6)	0.085	42 (100)	–
COPD	4 (19.0)	31 (15.4)	0.752	8 (19.0)	0.999
Atrial fibrillation	7 (33.3)	93 (46.3)	0.366	18 (42.9)	0.649
Porcelain aorta	0 (0.0)	1 (0.5)	0.999	0 (0)	–
Peripheral artery disease	1 (4.8)	35 (17.4)	0.212	1 (2.4)	0.999
On dialysis	3 (14.3)	2 (1.0)	0.007	1 (2.4)	0.104
Previous CAD	10 (47.6)	113 (56.2)	0.600	19 (45.2)	0.999
Previous PCI	9 (42.9)	74 (36.8)	0.758	9 (21.4)	0.139
Previous CABG	2 (9.5)	25 (12.4)	0.999	6 (14.3)	0.708
Previous MI	5 (23.8)	31 (15.4)	0.349	7 (16.7)	0.513
Previous AVR	0 (0)	4 (2.0)	0.999	1 (2.4)	0.999
Previous stroke	1 (4.8)	23 (11.4)	0.709	7 (16.7)	0.250
Previous pacemaker	2 (9.5)	32 (15.9)	0.749	5 (11.9)	0.999
Previous cancer	3 (14.3)	32 (15.9)	0.999	4 (9.5)	0.677
Echocardiographic data					
LVEF (%)	25.7 ± 6.6	31.7 ± 6.5	0.001	25.7 ± 6.3	0.989
AVA (cm^2)	0.7 ± 0.2	0.7 ± 0.2	0.511	0.7 ± 0.2	0.257
Mean transaortic gradient (mmHg)	36.7 ± 13.1	36.3 ± 13.8	0.880	31.0 ± 13.1	0.075
Severe aortic regurgitation	1 (4.8)	5 (2.5)	0.451	1 (2.4)	0.999
Pulmonary hypertension[a]	2 (9.5)	23 (11.4)	0.999	4 (9.5)	0.999

Data are given as mean ± standard deviation, median [interquartile range] or absolute numbers and (percentages)

pECMO prophylactic extracorporeal membrane oxygenation, *NYHA* New York Heart Association functional class, *COPD* chronic obstructive pulmonary disease, *CAD* coronary artery disease, *PCI* percutaneous coronary intervention, *CABG* coronary artery bypass graft, *MI* myocardial infarction, *AVR* aortic valve replacement, *LVEF* left ventricular ejection fraction, *AVA* aortic valve area

[a]Pulmonary arterial pressure on echocardiography ≥ 60 mmHg

or hybrid-operating room with a mean duration of pECMO support of 56 ± 39 min. No pECMO-related major vascular complications or life-threatening bleedings occurred (Table 2).

Impact of pECMO on procedural and in-hospital outcome

Procedural characteristics and in-hospital complications are depicted in Table 3. Median procedural time was longer with pECMO, in the entire population, (93 min vs. 65 min, $p<0.001$) as well as in the propensity-matched population (93 min vs. 70 min $p=0.001$). Device success was achieved in all cases with pECMO (100%, 21/21) compared to 91% (183/201) in the entire population ($p=0.230$) and remained comparable [(100%, 21/21) vs. 93% (38/42), $p=0.545$] in the matched population. In both groups, there was one case of ventricular rupture, requiring conversion to sternotomy. In the non-pECMO group, this patient underwent emergency ECMO as bridge-to-surgery. Five other patients in the entire population required emergency ECMO due to life-threatening complications. Of these, three cases were related to left ventricular pump failure with ventricular arrhythmias in one

Table 2 Prophylactic ECMO characteristics and ECMO-related complications

	pECMO+, $n=21$
pECMO characteristics	
Femoral access	21 (100)
Arterial cannula left side	12 (57)
Venous cannula left side	17 (81)
Arterial cannula	
15F/17F/19F/21F	15/4/1/1
Venous cannula	
17F/19F/21F/22F	2/6/10/3
pECMO time mean (min)	56 ± 39
pECMO-related complications	
Life-threatening bleeding	0 (0)
Major vascular complication	0 (0)

Data are given as mean ± standard deviation or absolute numbers and (percentages)

pECMO prophylactic extracorporeal membrane oxygenation

case and severe hypotension unresponsive to catecholamine administration in two cases.

Major bleedings were more frequent with pECMO [29% (6/21) vs. 9% (18/201); $p=0.015$] leading to more blood transfusions [≥ 2 units, 30% (6/21) vs. 10% (20/201); $p=0.019$]. In the matched population, only requirement of blood transfusions remained significantly higher with pECMO [30% (6/21) vs. 7% (3/41); $p=0.025$]. Overall, patients with pECMO had a prolonged hospital stay compared to patients without pECMO (9 days [7–14] vs. 7 days [5–10]; $p=0.024$), which remained as a trend after propensity matching (9 [7–14] days vs. 7 [5–9] days, $p=0.068$).

30-day and 1-year mortality according to pECMO

Overall, the crude mortality rate at 30-days was 7.7% (17/222). In the unmatched population, use of pECMO was associated with a higher rate (23.8% [3.2–40] vs. 5.5% [2.3–8.6]) and higher unadjusted risk of 30-day mortality

Table 3 Procedural characteristics and in-hospital complications according to pECMO

	pECMO+, $n=21$	Entire population		Matched population	
		pECMO−, $n=201$	p value	pECMO−, $n=42$	p value
Procedural data					
Balloon-expandable THV	14 (66.7)	131 (65.2)	0.999	28 (66.7)	1.000
Transfemoral access	15 (71.4)	146 (72.6)	0.999	31 (73.8)	0.999
Valve-in-valve	0 (0)	4 (2.0)	0.999	1 (2.4)	0.999
Device Success	21 (100)	183 (91.0)	0.230	39 (92.9)	0.545
Procedural time (min)	93.0 [79.0;114.0]	65.0 [53.0;81.0]	< 0.001	70.0 [52.8;86.0]	0.001
Contrast (ml)	98.5 [76.5;118.2]	100.0 [70.5;136.5]	0.594	98.5 [76.5;118.2]	0.684
Fluoroscopy time (min)	13.3 [9.9;18.7]	11.4 [8.0;16.9]	0.141	13.3 [9.9;18.7]	0.290
In-hospital complications					
Access site complication	2 (9.5)	6 (3.0)	0.169	2 (4.8)	0.595
Ventricular rupture	1 (4.8)	1 (0.5)	0.181	0 (0)	0.333
Pericardial tamponade	0 (0)	1 (0.5)	0.999	0 (0)	–
Emergency ECMO	0 (0)	6 (3.0)	0.999	2 (4.8)	0.548
Conversion to sternotomy	1 (4.8)	1 (0.5)	0.181	0 (0)	0.333
Life-threatening bleeding	3 (14.3)	8 (4.0)	0.073	1 (2.4)	0.104
Major bleeding	6 (28.6)	18 (9.0)	0.015	5 (11.9)	0.157
Minor bleeding	1 (4.8)	15 (7.5)	0.999	2 (4.8)	1.000
Blood transfusion (≥ 2 units)	6 (30.0)	20 (10.1)	0.019	3 (7.1)	0.025
Major vascular complication	3 (14.3)	11 (5.5)	0.136	3 (7.1)	0.391
Major stroke	1 (4.8)	3 (1.5)	0.330	1 (2.4)	0.999
Renal failure (AKIN 2/3)	8 (40.0)	46 (23.0)	0.105	9 (22.0)	0.241
Dialysis therapy	2 (10.0)	15 (7.5)	0.657	3 (7.1)	0.654
New permanent pacemaker	2 (10.0)	26 (13.0)	0.999	5 (12.2)	0.999
Days in hospital	9.0 [7.0;14.0]	7.0 [5.0;10.0]	0.024	7.0 [5.0;9.0]	0.068
Days on ICU	1.0 [1.0;4.0]	1.0 [1.0;2.0]	0.384	1.0 [1.0;2.0]	0.586

Data are given as median [interquartile range] or as frequencies (percentages)

pECMO prophylactic extracorporeal membrane oxygenation, *THV* transcatheter heart valve, *AKIN* acute kidney injury network classification, *ICU* intensive care unit

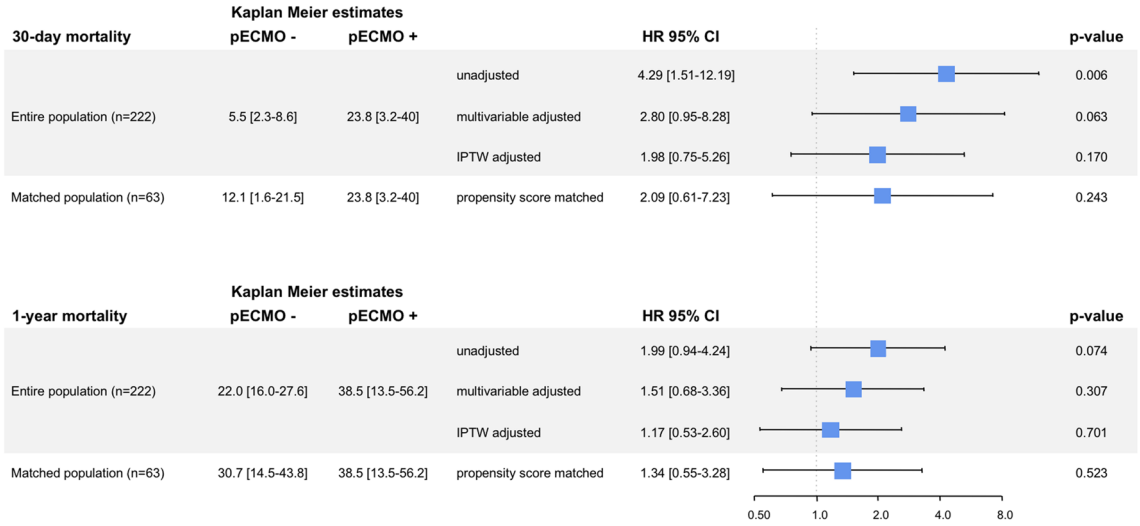

Fig. 2 Kaplan–Meier estimates and risk of 30-day and 1-year mortality according to use of pECMO. Event rates reported as Kaplan–Meier estimates and risk of mortality in the first 30 days and 1 year after TAVI according to the use of pECMO support in the entire population in an unadjusted model, after multivariable adjustment, IPTW (inverse probability of treatment weighting) and in the matched population of patients. pECMO: prophylactic extracorporeal membrane oxygenation; HR: hazard ratio, 95% CI: 95% confidence interval

compared to patients without pECMO (HR 95%CI 4.29 [1.51–12.19], $p = 0.006$, Fig. 2). However, after multivariable adjustment and further propensity score weighting, this increase in risk of 30-day mortality with pECMO was attenuated (Fig. 2). In the matched population, the difference in rate and risk of 30-day mortality was not significant (23.8% [95%CI 3.2–40] vs. 12.1% [95%CI 1.6–21.5], HR 95%CI 2.09 [0.61–7.23], $p = 0.243$) (Fig. 2). The overall, 1-year crude mortality rate was 23.0% (51/222). There was a trend towards a higher cumulative mortality (log-rank $p = 0.069$, Fig. 3) and higher rate and unadjusted risk of 1-year mortality with pECMO

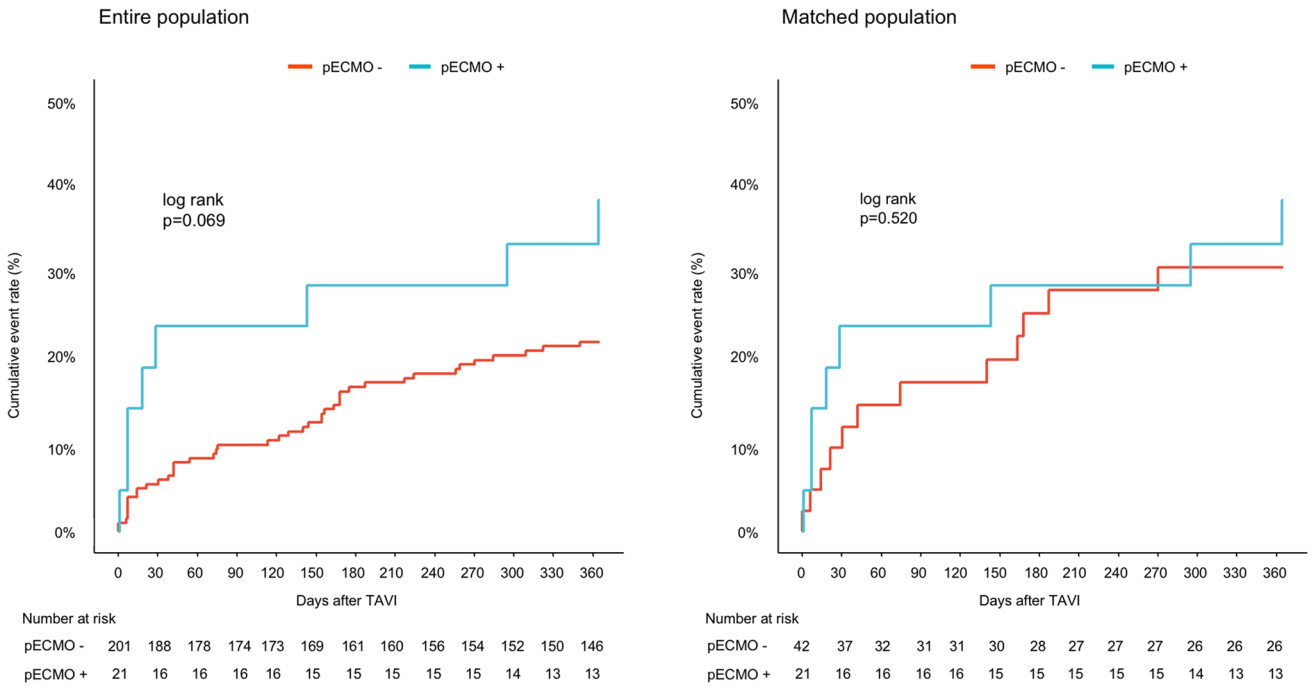

Fig. 3 Cumulative mortality 1 year after TAVI according to use of pECMO. Kaplan–Meier cumulative mortality rate during 1 year after TAVI in patients with pECMO (+) compared to patients without pECMO (−) in the entire population (left) and in the propensity-matched population (right). *TAVI* transcatheter aortic valve implantation, *pECMO* prophylactic extracorporeal membrane oxygenation

(38.5% [95%CI 13.5–56.2] vs. 22.0% [95%CI 16.0-27.6], HR 95% CI 1.99 [0.94–4.24], $p = 0.074$) (Fig. 2). In the matched population, there was no difference in rate and risk of 1-year mortality (38.5% [95%CI 13.5–56.2] vs. 30.7% [95%CI 14.5–43.8], HR 95% CI 1.34 [0.55–3.28], $p = 0.523$). Cumulative mortality after 1-year was comparable between patients with pECMO and matched controls (log-rank $p = 0.520$, Fig. 3).

Discussion

In this two-center observational study, the use of pECMO for full hemodynamic support during TAVI in patients with a reduced left ventricular ejection fraction was investigated. Using multivariable analysis and a propensity-matched cohort of patients to address the influence of an inherent selection bias, pECMO showed no positive impact on outcome during the first 30 days and 1 year after TAVI.

Role of hemodynamic support during TAVI

Over the last decade, increasing operator experience, iteration of devices and optimization of delivery systems has led to a decrease of in-hospital mortality in patients undergoing TAVI [17], especially in high-volume centers to about 1% [18]. Comprehensive preprocedural assessment with detailed imaging [19, 20] and adequate patient selection [21] has further improved safety and efficacy of TAVI. However, patients with dLVEF often accompanied by low-flow-low-gradient aortic stenosis remain a challenge with a poor prognosis after TAVI [4].

Because of higher vulnerability to hemodynamic deterioration during rapid left ventricular pacing, different strategies for mechanical circulatory support have been suggested for this subgroup of patients. In this scenario, some centers have reported use of prophylactic cardiopulmonary bypass during TAVI [10] while others have described the use of an intra-aortic balloon pump [22] or pECMO [11]. However, more systematic data on procedural success and patient outcome is not available and difficult to obtain because different devices have been used and indications for mechanical support often differ considerably. Therefore, in our study we focused on prophylactic mechanical support using pECMO and only included patients with reduced left ventricular ejection fraction.

Prophylactic ECMO in TAVI

Data on the use of pECMO during TAVI is limited with 8 [9] and 9 cases [11] described so far. Both studies found a beneficial effect of circulatory support on short-term patient outcome. In the present study, with the largest number of cases with pECMO during TAVI to date, we did not observe a favorable impact on survival. We only included patients with dLVEF and univariate analysis revealed significant differences in the risk profile of patients with pECMO indicating a strong influence of selection bias. In a recent study, Singh and colleagues detected a higher mortality rate in patients with mechanical support during TAVI even after propensity matching [23]. We used several statistical methods to compensate for imbalances in baseline characteristics using conventional multivariable adjustment, propensity score weighting and also a propensity-matched population. The unadjusted fourfold increased risk of 30-day mortality with pECMO was attenuated after multivariable adjustment and after propensity score weighting or propensity matching. Taken together, pECMO was not associated with an improved outcome in patients with dLVEF.

In the group without pECMO six patients (2.7%) required emergency ECMO implantation due to life-threatening complications, three of whom suffered a procedure-related death. This emphasizes the importance of an experienced heart team including interventional cardiologists, cardiac surgeons and anesthesiologists in specialized heart valve centers [24]. As expected procedural time was longer in patients with pECMO due to prior ECMO cannulation. Though, the overall mechanical support time was rather short with less than 1 h and decannulation of the ECMO system was performed safely in all cases directly after TAVI. We did not observe any weaning problems in patients with pECMO. However, there was no case of postprocedural moderate or severe aortic valve regurgitation, which may have affected the weaning process in patients with pECMO. The device success rate with pECMO was 100% which may reflect a more stable and controlled situation for the operators. Nevertheless, this conclusion remains speculative and although statistically not significant there were more periprocedural complications in the group with pECMO. Besides, it is important to emphasize that mechanical support in TAVI is associated with an increased length of hospital stay and higher cost of hospitalization [23]. In our study even after propensity matching there was a trend towards a longer hospital stay with pECMO. Interestingly, we did not detect any ECMO related vascular complication or ECMO related life-threatening bleeding. This may be explained by the rather short time of ECMO support and the elective cannulation prior to the procedure as compared to emergency indications. However, although not statistically significant 30-day mortality was nearly twice as high in the pECMO group. This trend of potential harm of pECMO in patients undergoing TAVI needs to be clarified in future studies.

Future implications

The present study raises some important questions on hemodynamic support during TAVI in the future. First, there must be a distinction between emergency and prophylactic circulatory support. For emergency scenarios a standardized back-up plan needs to be established in every TAVI center including an on-site cardiac surgery [25]. Emergency ECMO may be a feasible strategy for severe complications, however, mortality in this group of patients remains high [26]. Second, if prophylactic ECMO implantation does not have a beneficial effect in patients undergoing TAVI are there other devices which do? Or is this group of patients who requires hemodynamic support for TAVI implantation due to dLVEF a marginal group with a poor prognosis *per se*? Thereby it will be of special interest to further analyze subgroups i.e. patients with low-flow-low-gradient aortic valve stenosis with and without contractile reserve. Data on mortality rates in these patients mainly stem from studies of surgical aortic valve replacement showing a worse outcome in patients lacking contractile reserve [27, 28]. Similar, results were shown in a retrospective analysis of patients using dobutamine stress echocardiography prior to TAVI [29]. However, recently Ribeiro and colleagues could show that the absence of contractile reserve at baseline did not result in a worse outcome after TAVI [30]. In our study, we did not routinely assess contractile reserve prior to the procedure. These issues should be further evaluated in future studies. However, randomized trials in the field of ECMO are difficult to conduct. Overall, the ultimate decision for periprocedural support must remain at the discretion of the operator, and the present data may not justify routine use of pECMO in patients with dLVEF.

Limitations

One limitation is the retrospective nature of the study. Furthermore, the decision for pECMO was left at the discretion of the operator with no standardized selection of patients for pECMO support. In addition, administration of any vasopressors was not routinely recorded. In the present study, we only selected patients with dLVEF rather than expanding the inclusion to other indications i.e. hybrid procedures with PCI. Therefore, the sample size is comparatively small.

Conclusion

In this propensity-matched analysis in selected patients with dLVEF undergoing TAVI with pECMO support, use of pECMO does not seem to improve patient outcome. The routine use of pECMO in TAVI is currently not justified. This study forms the basis for future studies on mechanical support during TAVI, which are needed to identify those patients who benefit from circulatory support and to establish standardized protocols for the utilization of these devices.

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Compliance with ethical standards

Conflict of interest The authors have no conflict of interest to declare.

References

1. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG et al (2011) Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 364(23):2187–2198
2. Levy F, Laurent M, Monin JL, Maillet JM, Pasquet A, Le Tourneau T et al (2008) Aortic valve replacement for low-flow/low-gradient aortic stenosis operative risk stratification and long-term outcome: a European multicenter study. J Am Coll Cardiol 51(15):1466–1472
3. Lauten A, Zahn R, Horack M, Sievert H, Linke A, Ferrari M et al (2012) Transcatheter aortic valve implantation in patients with low-flow, low-gradient aortic stenosis. JACC Cardiovasc Interv 5(5):552–559
4. Lauten A, Figulla HR, Mollmann H, Holzhey D, Kotting J, Beckmann A et al (2014) TAVI for low-flow, low-gradient severe aortic stenosis with preserved or reduced ejection fraction: a subgroup analysis from the German Aortic Valve Registry (GARY). EuroIntervention 10(7):850–859
5. Amabile N, Agostini H, Gilard M, Eltchaninoff H, Iung B, Donzeau-Gouge P et al (2014) Impact of low preprocedural transvalvular gradient on cardiovascular mortality following TAVI: an analysis from the FRANCE 2 registry. EuroIntervention 10(7):842–849
6. Schymik G, Tzamalis P, Herzberger V, Bergmann J, Bramlage P, Wurth A et al (2017) Transcatheter aortic valve implantation in patients with a reduced left ventricular ejection fraction: a single-centre experience in 2000 patients (TAVIK Registry). Clin Res Cardiol 106(12):1018–1025
7. Tamburino C, Capodanno D, Ramondo A, Petronio AS, Ettori F, Santoro G et al (2011) Incidence and predictors of early and late mortality after transcatheter aortic valve implantation in 663 patients with severe aortic stenosis. Circulation 123(3):299–308
8. Holmes DR Jr, Mack MJ, Kaul S, Agnihotri A, Alexander KP, Bailey SR et al (2012) 2012 ACCF/AATS/SCAI/STS expert consensus document on transcatheter aortic valve replacement. J Am Coll Cardiol 59(13):1200–1254
9. Seco M, Forrest P, Jackson SA, Martinez G, Andvik S, Bannon PG et al (2014) Extracorporeal membrane oxygenation for very high-risk transcatheter aortic valve implantation. Heart Lung Circ 23(10):957–962
10. Drews T, Pasic M, Buz S, Dreysse S, Klein C, Kukucka M et al (2015) Elective use of femoro-femoral cardiopulmonary bypass during transcatheter aortic valve implantation. Eur J Cardiothorac Surg 47(1):24–30; discussion
11. Husser O, Holzamer A, Philipp A, Nunez J, Bodi V, Muller T et al (2013) Emergency and prophylactic use of miniaturized veno-arterial extracorporeal membrane oxygenation in transcatheter aortic valve implantation. Catheter Cardiovasc Interv 82(4):E542–E551

12. Barbaro RP, Odetola FO, Kidwell KM, Paden ML, Bartlett RH, Davis MM et al (2015) Association of hospital-level volume of extracorporeal membrane oxygenation cases and mortality. Analysis of the extracorporeal life support organization registry. Am J Respir Crit Care Med 191(8):894–901
13. Napp LC, Kuhn C, Hoeper MM, Vogel-Claussen J, Haverich A, Schafer A et al (2016) Cannulation strategies for percutaneous extracorporeal membrane oxygenation in adults. Clin Res Cardiol 105(4):283–296
14. Arlt M, Philipp A, Zimmermann M, Voelkel S, Amann M, Bein T et al (2009) Emergency use of extracorporeal membrane oxygenation in cardiopulmonary failure. Artif Organs 33(9):696–703
15. Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH et al (2013) Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Thorac Cardiovasc Surg 145(1):6–23
16. McCaffrey DF, Ridgeway G, Morral AR (2004) Propensity score estimation with boosted regression for evaluating causal effects in observational studies. Psychol Methods 9(4):403–425
17. Gaede L, Blumenstein J, Kim WK, Liebetrau C, Dorr O, Nef H et al (2017) Trends in aortic valve replacement in Germany in 2015: transcatheter versus isolated surgical aortic valve repair. Clin Res Cardiol 106(6):411–419
18. Husser O, Kim WK, Pellegrini C, Holzamer A, Walther T, Mayr PN et al (2017) Multicenter Comparison of Novel Self-Expanding Versus Balloon-Expandable Transcatheter Heart Valves. JACC Cardiovasc Interv 10(20):2078–2087
19. Husser O, Holzamer A, Resch M, Endemann DH, Nunez J, Bodi V et al (2013) Prosthesis sizing for transcatheter aortic valve implantation–comparison of three dimensional transesophageal echocardiography with multislice computed tomography. Int J Cardiol 168(4):3431–3438
20. Bernhardt P, Rodewald C, Seeger J, Gonska B, Buckert D, Radermacher M et al (2016) Non-contrast-enhanced magnetic resonance angiography is equal to contrast-enhanced multislice computed tomography for correct aortic sizing before transcatheter aortic valve implantation. Clin Res Cardiol 105(3):273–278
21. Bax JJ, Delgado V, Bapat V, Baumgartner H, Collet JP, Erbel R et al (2014) Open issues in transcatheter aortic valve implantation. Part 1: patient selection and treatment strategy for transcatheter aortic valve implantation. Eur Heart J 35(38):2627–2638
22. Shreenivas SS, Lilly SM, Szeto WY, Desai N, Anwaruddin S, Bavaria JE et al (2015) Cardiopulmonary bypass and intra-aortic balloon pump use is associated with higher short and long term mortality after transcatheter aortic valve replacement: a PARTNER trial substudy. Catheter Cardiovasc Interv 86(2):316–322
23. Singh V, Patel SV, Savani C, Patel NJ, Patel N, Arora S et al (2015) Mechanical circulatory support devices and transcatheter aortic valve implantation (from the National Inpatient Sample). Am J Cardiol 116(10):1574–1580
24. Seiffert M, Conradi L, Baldus S, Schirmer J, Blankenberg S, Reichenspurner H et al (2013) Severe intraprocedural complications after transcatheter aortic valve implantation: calling for a heart team approach. Eur J Cardiothorac Surg 44(3):478–484
25. Kim WK, Hamm CW (2018) Transcatheter aortic valve implantation in Germany. Clin Res Cardiol 107(Suppl 2):81–87
26. Trenkwalder T, Pellegrini C, Holzamer A, Philipp A, Rheude T, Michel J et al (2017) Emergency extracorporeal membrane oxygenation in transcatheter aortic valve implantation: a two-center experience of incidence, outcome and temporal trends from 2010 to 2015. Catheter Cardiovasc Interv
27. Tribouilloy C, Levy F, Rusinaru D, Gueret P, Petit-Eisenmann H, Baleynaud S et al (2009) Outcome after aortic valve replacement for low-flow/low-gradient aortic stenosis without contractile reserve on dobutamine stress echocardiography. J Am Coll Cardiol 53(20):1865–1873
28. Quere JP, Monin JL, Levy F, Petit H, Baleynaud S, Chauvel C et al (2006) Influence of preoperative left ventricular contractile reserve on postoperative ejection fraction in low-gradient aortic stenosis. Circulation 113(14):1738–1744
29. Hayek S, Pibarot P, Harzand A, Cheng JW, Gay H, Chrysohoou C et al (2015) Dobutamine stress echocardiography for risk stratification of patients with low-gradient severe aortic stenosis undergoing TAVR. JACC Cardiovasc Imaging 8(3):380–382
30. Ribeiro HB, Lerakis S, Gilard M, Cavalcante JL, Makkar R, Herrmann HC et al (2018) Transcatheter Aortic Valve Replacement in Patients With Low-Flow, Low-Gradient Aortic Stenosis: The TOPAS-TAVI Registry. J Am Coll Cardiol 71(12):1297–1308