Check for updates

Received: 8 January 2024 | Revised: 9 April 2024 | Accepted: 9 May 2024

DOI: 10.1111/aor.14775

Artificial Organs WILEY

MAIN TEXT

Stroke outcomes following durable left ventricular assist device implant in patients bridged with micro-axial flow pump: Insights from a large registry

Guglielmo Gallone[1] | Daniel Lewin[2,3] | Sebastian Rojas Hernandez[4] | Alexander Bernhardt[5] | Michael Billion[6] | Anna Meyer[7] | Ivan Netuka[8] | J-J Kooij[9] | Marina Pieri[10] | Mariusz K. Szymanski[11] | Christian H. Moeller[12] | Payam Akhyari[13] | Khalil Jawad[14] | Ihor Krasivskyi[15] | Bastian Schmack[16] | Gloria Färber[17] | Marta Medina[18] | Assad Haneya[19] | Daniel Zimpfer[20] | Gaik Nersesian[2,21] | Pia Lanmueller[2,3,21] | Antonio Spitaleri[22] | Mehmet Oezkur[18] | Ilija Djordjevic[15] | Diyar Saeed[14] | Massimo Boffini[22] | Julia Stein[3] | F. Gustafsson[12] | Anna Mara Scandroglio[10] | Gaetano Maria De Ferrari[1] | Bart Meyns[9] | Steffen Hofmann[6] | Jan Belohlavek[23,24] | Jan Gummert[4] | Mauro Rinaldi[22] | Evgenij V. Potapov[2,3,21] | Antonio Loforte[22]

Correspondence
G. Gallone and A. Loforte, City of Health and Science Hospital, University of Turin, Corso Bramante 88/90, Turin, Italy.
Email: guglielmo.gallone@gmail.com and antonino.loforte@unito.it

Abstract

Background: Stroke after durable left ventricular assist device (d-LVAD) implantation portends high mortality. The incidence of ischemic and hemorrhagic stroke and the impact on stroke outcomes of temporary mechanical circulatory support (tMCS) management among patients requiring bridge to d-LVAD with micro-axial flow-pump (mAFP, Abiomed) is unsettled.

Methods: Consecutive patients, who underwent d-LVAD implantation after being bridged with mAFP at 19 institutions, were retrospectively included. The incidence of early ischemic and hemorrhagic stroke after d-LVAD implantation (<60 days) and association of pre-d-LVAD characteristics and peri-procedural management with a specific focus on tMCS strategies were studied.

Results: Among 341 patients, who underwent d-LVAD implantation after mAFP implantation (male gender 83.6%, age 58 [48–65] years, mAFP 5.0/5.5 72.4%), the early ischemic stroke incidence was 10.8% and early hemorrhagic stroke 2.9%. The tMCS characteristics (type of mAFP device and access, support duration, upgrade from intra-aortic balloon pump, ECMELLA, ECMELLA at d-LVAD implantation, hemolysis, and bleeding) were not associated with ischemic stroke after d-LVAD implant. Conversely, the device model (mAFP 2.5/CP vs. mAFP 5.0/5.5: HR 5.6, 95%CI 1.4–22.7, $p = 0.015$), hemolysis on mAFP support (HR 10.5,

G. Gallone and D. Lewin contributed equally to writing this manuscript.

For affiliations refer to page 11.

© 2024 International Center for Artificial Organ and Transplantation (ICAOT) and Wiley Periodicals LLC.

95% CI 1.3–85.3, $p=0.028$) and ECMELLA at d-LVAD implantation (HR 5.0, 95% CI 1.4–18.7, $p=0.016$) were associated with increased risk of hemorrhagic stroke after d-LVAD implantation. Both early ischemic (HR 2.7, 95% CI 1.9–4.5, $p<0.001$) and hemorrhagic (HR 3.43, 95% CI 1.49–7.88, $p=0.004$) stroke were associated with increased 1-year mortality.

Conclusions: Among patients undergoing d-LVAD implantation following mAFP support, tMCS characteristics do not impact ischemic stroke occurrence, while several factors are associated with hemorrhagic stroke suggesting a proactive treatment target to reduce this complication.

KEYWORDS

bridge strategy, impella, left ventricular assist device, micro-axial flow pump, outcomes, stroke

1 | INTRODUCTION

The utilization of durable left ventricular assist devices (d-LVADs) has witnessed a substantial rise in recent years, paralleled by remarkable advancements in their design and clinical outcomes.[1,2] These durable mechanical circulatory support systems have transformed the management of end-stage heart failure patients, offering an increasingly effective therapeutic option even among the most critically ill individuals (INTERMACS 1-2).[1,2] This growing success in d-LVAD implementation among patients in cardiogenic shock has given rise to a notable increase in the utilization of temporary mechanical circulatory support devices (tMCS) as a bridge to d-LVAD therapy.[3–5] Micro-axial flow pumps (mAFP devices, Abiomed) have emerged as an increasing choice.[6–9] This evolving landscape of circulatory support strategies has introduced new complexities in the peri-procedural care of d-LVAD recipients, necessitating focused attention on optimal management and the implications for early d-LVAD-related outcomes.

The peri-procedural course of d-LVAD implantation in patients supported by mAFP devices presents unique management challenges and requires a deeper understanding of its impact on clinical outcomes. Despite the expanding experience with d-LVADs, there remains a paucity of information regarding the specific effects of mAFP support on early d-LVAD-related outcomes, making it imperative to investigate this aspect comprehensively. Early neurological complications, particularly strokes, remain a concerning issue in the d-LVAD population, contributing to increased mortality and disability.[1,10] While the temporal trends suggest improved early neurological outcomes, the occurrence of stroke events remains prevalent, prompting further exploration of potential risk factors.[1,10–12]

One notable concern surrounding the use of mAFP devices is their association with an increased risk of stroke.[13] However, the extent to which the comprehensive management of mAFP support including pump model, support duration, sequential and/or combined tMCS use and complications while on support may relate to stroke risk following d-LVAD implantation remains a subject of uncertainty and warrants detailed investigation. Clarifying the relationship between the pre-procedural management strategy and post-d-LVAD stroke risk among patients requiring mAFP bridging is crucial for optimizing patient care and refining the management of tMCS in clinical practice. Therefore, the primary objective of this investigation is to characterize the incidence of stroke among patients requiring mAFP support as a bridge to d-LVAD therapy with a focus on the comprehensive tMCS strategy and pre-operative clinical course.

2 | METHODS

All consecutive patients with advanced HF undergoing implantation of a continuous-flow d-LVAD with previous circulatory support mAFP temporary LVAD between January 2017 and December 2022, at 19 European institutions were retrospectively analyzed.

Data on patient history, pre-d-LVAD temporary mechanical circulatory support use, management and complications, d-LVAD peri-procedural course, and outcomes were collected in a pre-designed dataset. Several variables relating to the mAFP strategy, management, and complications were evaluated, including the type of mAFP device, the type of mAFP access, the duration of support, the need for an upgrade (from an intra-aortic balloon pump to a mAFP or from a 2.5/CP mAFP to a 5.0/5.5 mAFP), the need for concomitant use of an extracorporeal membrane oxygenation (ECMELLA strategy), and the need for ECMELLA support at the time of d-LVAD implantation, along with the development of hemolysis and blood loss on support.

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

The study protocol was approved by the individual Health Research Ethics Boards.

2.1 | Study outcomes

The co-primary outcomes analyzed in the presented study were ischemic stroke and hemorrhagic stroke occurring early post-d-LVAD implant (in-hospital and up to 60 days).

The association of early ischemic and hemorrhagic strokes with the occurrence of all-cause death, heart transplant, pump thrombosis, gastro-intestinal bleeding, and driveline infection up to 1-year was assessed. If patients underwent heart transplantation, d-LVAD explantation, or deceased, follow-up was censored.

Moreover, the association with early severe RV failure (temporary RVAD implant within 30 days) after d-LVAD was analyzed.

Outcomes were defined according to the updated INTERMACS definitions of d-LVAD adverse events.[14] Specifically, ischemic stroke was defined as a Type 1a and hemorrhagic stroke as a Type 1b or 1c neurological dysfunction event.

Hemolysis on mAFP support was defined as plasma-free hemoglobin >20 mg/dL or LDH >2.5-fold the upper reference limit.[14]

2.2 | Statistical analysis

Categorical variables are expressed as number and percentages, continuous variables are expressed as mean ± standard deviation or median and interquartile range (IQR) as appropriate. Unpaired *t*-test or nonparametric Mann–Whitney *U*-test was used for comparisons of continuous variables and chi-square test was used for categorical variables.

Kaplan–Meier survival curves and log-rank *p*-values were used to evaluate the incidence of early ischemic and hemorrhagic strokes and of the other study outcomes.

Univariate and multivariate Cox regression analyses were performed to identify the outcome predictors. The covariates associated with the outcome of interest at univariate analysis with a $p < 0.05$ were considered for inclusion in the multivariate models. Considering the low number of events, the tMCS characteristics associated with the outcome at univariate analysis were prioritized for inclusion in the multivariate models. Results are presented as hazard ratio (HR) and 95% confidence intervals (CIs).

A $p < 0.05$ was considered statistically significant. Statistical analyses were conducted using SPSS (version 24.0, SPSS Inc., Chicago, Illinois, US) and STATA (version 17, StataCorp, College Station, Texas).

3 | RESULTS

3.1 | Study population

Overall, the study population consisted of 341 patients, who underwent d-LVAD implant with previous mAFP support. Patient characteristics prior to d-LVAD implant are depicted in Table 1. The median age was 58 years (interquartile range [IQR] 48–65 years), 83.6% were male, 60.1% presented with ischemic cardiomyopathy, and 11.4% had a prior stroke in their medical history. Almost one in three patients experienced cardiac arrest prior to mAFP placement (30.6%).

3.2 | Temporary mechanical circulatory support characteristics

The type, management, and complications of tMCS strategy are reported in Table 2. Overall, 2 (0.6%) patients received an mAFP 2.5, 92 (27.0%) received an mAFP CP, 155 (45.5%) received an mAFP 5.0, and 92 (27.0%) received an mAFP 5.5. mAFP was preferentially placed through the trans-axillary access (71.8%). 9.1% had an intra-aortic balloon pump prior to mAFP implantation and, among patients with an mAFP 5.0/5.5, in 39 (15.5%) cases the device was placed as an upgrade from a less potent mAFP device (2.5 or CP). An ECMELLA strategy was deemed necessary in 133 (40.5%, $n = 79$ mAFP 5.0/5.5; $n = 54$ mAFP 2.5/CP) patients, and 20.6% were still on ECMO support at d-LVAD implant. Median mAFP support duration was 9 (IQR 5–14) days (Figure 1).

The patient course on mAFP support is detailed in Table 1. Median max. vasoactive-inotropic score on support was 3.7 (IQR 0–7.8), 43.1% required mechanical ventilation and 29.1% required renal replacement therapy. While on mAFP support, 32.4% of the patients were mobilized out of bed.

Regarding device complications, hemolysis was frequently developed (40.8%), 38.1% had more than 1 L of estimated blood loss while on mAFP support, and 73.4% required blood transfusion.

At the last evaluation prior to d-LVAD implant, pulmonary congestion (mean pulmonary artery pressure ≥25 mm Hg) was present in 58.5%, low cardiac index (<2.2 L/min/m^2) in 57.7% and high central venous pressure (≥15 mm Hg) in 8.5% of the patients. Moreover, 10.7% of the patients had elevated lactates (>2 mmol/L), 19.2%

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1 Baseline characteristics, mAFP support course, and peri-procedural d-LVAD implant characteristics in the overall cohort and stratified by ischemic stroke and hemorrhagic stroke occurrence.

	Overall ($n=341$)	No ischemic stroke ($n=307$)	Ischemic stroke ($n=34$)	*p*-value	No hemorrhagic stroke ($n=332$)	Hemorrhagic stroke ($n=9$)	*p*-value
Patient characteristics							
Age (years)	58 (48–65)	57 (48–65)	61 (48–64)	0.752	58 (48–65)	50 (42–52)	0.023
Male sex (%)	285 (83.6)	257 (83.7)	28 (82.4)	0.498	281 (84.6)	4 (44.4)	**0.008**
BMI (kg/m^2)	26 (24–29)	26 (24–29)	26 (24–29)	0.562	26 (24–29)	31 (25–36)	0.072
Ischemic cardiomyopathy (%)	205 (60.1)	180 (58.6)	25 (73.5)	0.078	202 (60.8)	3 (33.3)	0.125
Prior cardiac surgery (%)	57 (17.9)	51 (17.7)	6 (19.4)	0.490	56 (18.1)	1 (11.1)	0.501
Prior stroke (%)	36 (11.4)	29 (10.2)	7 (2.2)	0.054	35 (11.3)	1 (12.5)	0.623
Diabetes (%)	101 (30)	88 (29)	13 (38.2)	0.180	100 (30.5)	1 (11.1)	0.193
Atrial fibrillation (%)	128 (37.5)	119 (38.8)	9 (26.5)	0.110	126 (38.0)	2 (22.2)	0.278
Peripheral artery disease (%)	31 (9.2)	29 (9.6)	2 (5.9)	0.369	31 (9.2)	0 (0)	0.414
Patient course on mAFP support							
Mechanical ventilation (%)	143 (43.1)	128 (42.8)	15 (45.5)	0.455	138 (42.7)	5 (55.6)	0.332
Mobilization out of the bed (%)	132 (32.4)	155 (33.3)	11 (23.4)	0.183	99 (32.8)	1 (12.2)	0.095
Vasoactive-inotropic score (points)	3.7 (0–7.8)	3.6 (0–7.9)	4.4 (0–7.8)	0.901	3.6 (0–7.6)	9.0 (1.8–14.6)	0.054
Renal replacement therapy (%)	99 (29.1)	90 (29.4)	9 (26.5)	0.446	93 (28.1)	6 (66.7)	**0.020**
Hemoglobin (g/dL)	9.5 (8.5–10.5)	9.5 (8.6–10.6)	8.9 (8.3–10.3)	0.072	9.5 (8.5–10.5)	10.1 (9.2–10.8)	0.295
WBC ($n\times10^9$/L)	11.1 (8.7–14.6)	11 (8.7–14.6)	12.1 (8.9–14.4)	0.503		13.5 (9.6–20.7)	0.147
Platelets ($n\times10^9$/L)	126 (84–192)	126 (84–196)	116 (82–167)	0.326	127 (86–193)	59 (51–111)	**0.008**
Lactates (mmol/L)	1.10 (0.78–1.51)	1.11 (0.80–1.56)	1.0 (0.70–1.29)	0.055	1.10 (0.78–1.50)	1.30 (1.00–1.68)	0.340
Direct bilirubin (mg/dL)	1.1 (0.6–2.7)	1.1 (0.6–2.9)	1.16 (0.65–2.08)	0.473	1.1 (0.6–2.6)	4.4 (1.3–9.2)	**0.034**
Hemolysis (%)	127 (40.8)	113 (40.4)	14 (45.2)	0.370	120 (39.6)	7 (87.5)	**0.009**
C reactive protein (mg/dL)	8.8 (3.8–20.9)	8.7 (3.8–20.2)	11 (4.1–29.9)	0.385	8.7 (3.8–20.4)	12.5 (7.2–38.6)	0.351
Albumin (mg/dL)	2.7 (2.2–3.1)	2.7 (2.2–3.2)	2.7 (2.3–3.0)	0.285	2.7 (2.2–3.1)	2.2 (2.1–2.5)	0.041
AST (UI/L)	63 (38–134)	62 (37–129)	63 (41–171)	0.420	62 (38–129)	174 (66–1300)	**0.039**
INR (IU/L)	1.2 (1.1–1.3)	1.2. (1.1–1.4)	1.1 (1.1–1.3)	0.058	1.2 (1.1–1.3)	1.2 (1.1–1.4)	0.602
Creatinine (mg/dL)	1.1 (0.8–1.7)	1.1 (0.8–1.7)	1.0 (0.9–1.7)	0.600	1.10 (0.82–1.71)	0.88 (0.72–2.49)	0.644
mPAP (mm Hg)	27 (19–38)	26 (18–38)	34 (25–71)	**0.041**	27 (19–38)	28 (27–29)	0.903
PAPi	1.7 (0.9–3.0)	1.6 (0.9–3.0)	1.7 (1.1–4.0)	0.927	1–7 (0.9–3.0)	2.2 (1.5–2.6)	0.595
CVP (mm Hg)	10 (7–15)	11 (7–15)	10 (5–15)	0.542	10 (7–15)	15 (10–19)	0.127
Cardiac index (L/min/m^2)	2.0 (1.6–2.7)	2.0 (1.6–2.6)	2.2 (1.6–3.8)	0.284	2.0 (1.6–2.7)	2.6 (2.6–2.6)	0.523
Peri-procedural characteristics							
Mini-invasive implant (%)	24 (7.7)	23 (8.1)	1 (3.6)	0.341	23 (7.5)	1 (25)	0.275
Implant on CPB (%)	241 (72.8)	218 (73.2)	23 (69.7)	0.405	237 (73.6)	4 (44.4)	0.065

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1 (Continued)

	Overall ($n=341$)	No ischemic stroke ($n=307$)	Ischemic stroke ($n=34$)	*p*-value	No hemorrhagic stroke ($n=332$)	Hemorrhagic stroke ($n=9$)	*p*-value
Surgical time (min)	239 (180–293)	239 (178–291)	243 (183–310)	0.402	239 (180–294)	241 (183–271)	0.978
Concomitant cardiac surgery (%)	74 (21.7)	64 (20.8)	10 (29.4)	0.175	70 (94.6)	4 (44.4)	0.107
Blood loss during LVAD implant (mL)	610 (325–1200)	645 (337–1250)	572 (260–910)	0.259	610 (322–1200)	915 (551–1375)	0.611
RVAD implant (%)	72 (21.1)	66 (21.5)	6 (17.6)	0.394	68 (20.5)	4 (44.4)	0.098
RVAD duration (days)	17 (10–24)	16 (10–23)	24 (9–27)	0.435	18 (10–24)	15 (0–34)	0.536
Red blood cell transfusion (units)	5 (2–8)	5 (2–8)	4 (2–8)	0.664	5 (2–8)	10 (7–14)	**0.004**
Rethoracotomy (%)	80 (23.5)	70 (22.8)	10 (29.4)	0.252	76 (22.9)	4 (44.4)	0.135

Abbreviations: BMI, body mass index; CPB, cardiopulmonary bypass; CVP, central venous pressure; d-LVAD, durable LVAD; mPAP, mean pulmonary artery pressure; PAPi, pulmonary artery pulsatility index; RVAD, right ventricular assist device; WBC, white blood cells.

Bold values indicates level of significance was set at $p<0.05$

had renal damage (creatinine >2 mg/dL) and 11.0% of the patients had severe anemia (hemoglobin <8.0 g/dL).

3.3 | Early stroke outcomes

Following d-LVAD implant, 34 early ischemic and 9 early hemorrhagic strokes occurred. The Kaplan–Meier estimates of early ischemic stroke occurrence was 10.8% and of early hemorrhagic stroke 2.9% (Figure 2). Univariate predictors of ischemic and hemorrhagic strokes are reported in Table 3.

Ischemic stroke was associated with history of prior stroke (HR 2.34, 95% CI 1.01–5.40, $p=0.047$), with severe anemia prior to d-LVAD implant (HR 2.36, 95% CI 1.02–5.43, $p=0.044$) and with mean pulmonary artery pressure prior to d-LVAD implant (HR 1.03 per mm Hg increase, 95% CI 1.01–1.04, $p=0.005$). The mAFP strategy, management, and complications did not affect ischemic stroke occurrence (Table 3 and Figure 3). At multivariate analysis, among the three univariate predictors of ischemic stroke, severe anemia prior to d-LVAD implant remained the only independent predictor of ischemic stroke following d-LVAD implant (HR 2.4, 95% CI 1.1–5.5, $p=0.047$).

Hemorrhagic stroke was associated with patient-related factors including female sex, higher body mass index, and cardiac arrest prior to mAFP implant (Table 3). Moreover, several factors related to the tMCS characteristics including type of mAFP device (mAFP 2.5/CP vs. mAFP 5.0/5.5: HR 5.6, 95% CI 1.4–22.7, $p=0.015$), hemolysis on mAFP support (HR 10.5, 95% CI 1.3–85.3, $p=0.028$), and ECMELLA at the time of d-LVAD implantation (HR 5.0, 95% CI 1.4–18.7, $p=0.016$) were associated with increased risk of hemorrhagic stroke following d-LVAD implant (Figure 2). Due to the low outcome rate, multivariate analysis was limited to the univariate significant predictors pertaining to tMCS management (mAFP device type, ECMO at LVAD implant, hemolysis on mAFP support). Among these, the mAFP device remained the only independent predictor of hemorrhagic stroke following d-LVAD implant (HR 5.5, 95% CI 1.1–27.8, $p=0.039$). Notably, hemolysis was more common among patients with mAFP 2.5/CP versus mAFP 5.0/5.5 models (58.1% vs. 34.2%, $p<0.001$) and was associated with higher risk of severe thrombocytopenia (platelets count $<50\times10^9$/L) (46.5% vs. 31.0%, $p=0.004$), that was itself a predictor of hemorrhagic stroke (HR 5.3, 95% CI 1.07–26.3, $p=0.041$). Also, renal replacement therapy during mAFP support and red blood cells transfusion post-d-LVAD implant were associated with hemorrhagic stroke (Table 3).

3.4 | Association of early ischemic and hemorrhagic strokes with other d-LVAD-related outcomes

All-cause mortality on d-LVAD support at 1-year was different between patients with versus without early ischemic stroke (51.6% vs. 25.4%, $p<0.001$) and between patients with versus without early hemorrhagic stroke (70.4% vs. 28.9%, $p=0.004$). Both early ischemic (HR 2.7, 95% CI 1.9–4.5, $p<0.001$) and hemorrhagic (HR 3.43, 95% CI 1.49–7.88, $p=0.004$) strokes were associated with 1-year mortality (Table 4 and Figure 4).

Early severe right ventricular failure occurrence was similar regardless of stroke status (Table 4).

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 2 Temporary mechanical circulatory support strategies and complications bridge to d-LVAD in the overall cohort and stratified by ischemic stroke and hemorrhagic stroke occurrence.

MCS characteristics									
	Overall (*n* = 341)	**No ischemic stroke (*n* = 307)**	**Ischemic stroke (*n* = 34)**	**HR (95% CI)**	***p*-value**	**No hemorrhagic stroke (*n* = 332)**	**Hemorrhagic stroke (*n* = 9)**	**HR (95% CI)**	***p*-value**
mAFP 2.5/CP (vs. 5.0/5.5)	93 (27.6)	84 (24.6)	10 (29.4)	1.20 (0.57–2.51)	0.628	88 (26.5)	6 (66.7)	5.62 (1.41–22.71)	**0.015**
Trans-axillary access (%) (vs. femoral)	245 (71.8)	221 (72)	24 (70.6)	0.97 (0.45–2.08)	0.930	241 (72.6)	4 (44.4)	0.29 (0.08–1.09)	0.068
mAFP support duration (days)	9 (5–14)	9 (5–14)	8 (4–11)	0.95 (0.90–1.01)	0.081	9 (5–14)	8 (5–12)	0.97 (0.88–1.06)	0.521
Cardiac arrest prior to mAFP (%)	103 (30.6)	91 (30.0)	12 (35.3)	1.36 (0.67–2.75)	0.389	96 (29.3)	7 (77.8)	8.41 (1.75–40.47)	**0.008**
Blood loss during mAFP implant (mL)	155 (0–1315)	150 (0–1190)	687 (95–1637)	1.00 (1.00–1.00)	0.918	150 (0–1210)	1350 (1350–1350)	1.00 (0.99–1.01)	0.961
Upgrade from IABP (%)	31 (9.1)	28 (8.2)	3 (8.8)	0.94 (0.29–3.07)	0.917	29 (8.7)	2 (22.2)	2.77 (0.57–13.31)	0.205
Upgrade from mAFP 2.5/CP to 5.0/5.5 (%)	39 (15.1)	32 (13.7)	7 (26.9)	2.10 (0.89–5.01)	0.092	39 (15.4)	0 (0)	0.04 (0.01–1570)	0.548
ECMELLA (%)	133 (40.5)	118 (39.9)	15 (46.9)	1.40 (0.70–2.80)	0.343	127 (39.8)	6 (66.7)	3.02 (0.76–12.08)	0.118
ECMO duration (days)	7 (4.11)	7 (4–11)	6 (4–8)	0.99 (0.92–1.06)	0.726	7 (4.10)	8 (3–16)	1.01 (0.05–1.06)	0.867
ECMO support at LVAD implant	64 (20.6)	54 (19.3)	10 (32.3)	2.02 (0.95–4.30)	0.067	59 (19.5)	5 (55.6)	5.03 (1.35–18.72)	**0.016**
HeartWare LVAD (%) (vs. HeartMate III)	129 (37.9)	113 (36.9)	16 (47.1)	1.75 (0.90–3.45)	0.100	124 (37.5)	5 (55.6)	3.13 (0.79–12.5)	0.103

Abbreviations: CI, confidence interval; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump; HR, hazard ratio. Other abbreviations as in Table 1.

Bold values indicates level of significance was set at $p<0.05$

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

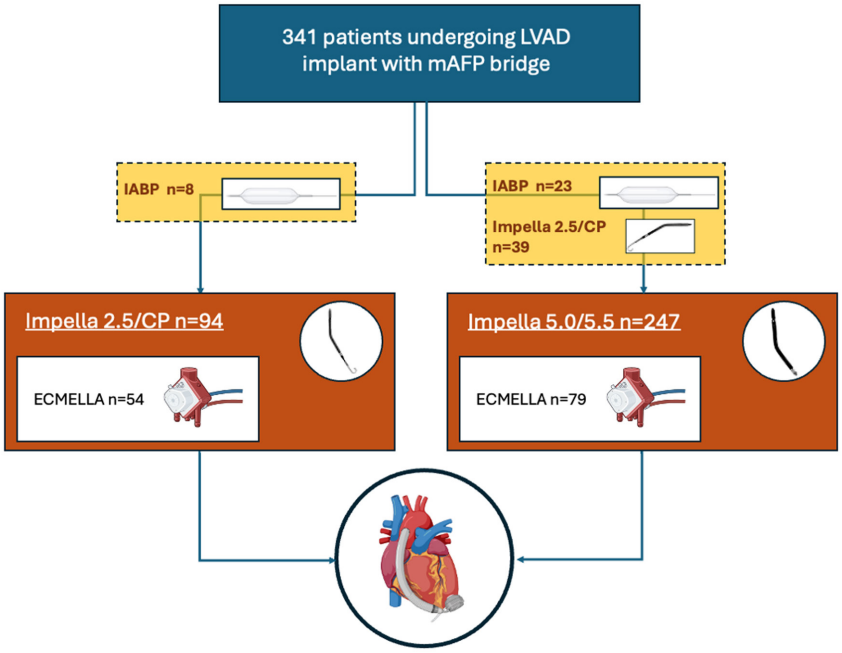

FIGURE 1 Study flow chart of tMCS strategies bridge to d-LVAD.

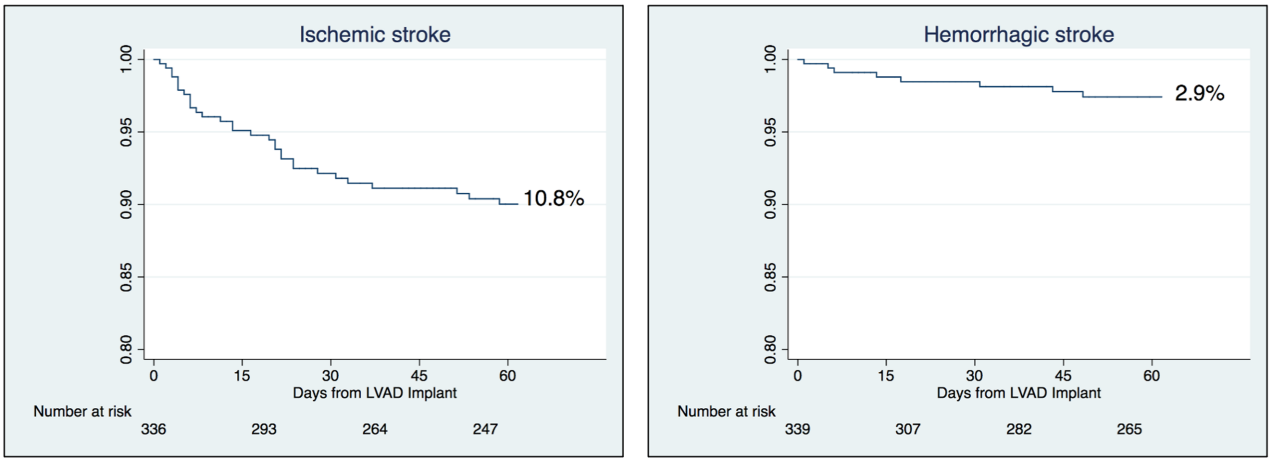

FIGURE 2 Kaplan–Meier estimates for the occurrence of ischemic (left) and hemorrhagic (right) stroke early after d-LVAD implant (in-hospital and up to 60 days) among patients requiting mAFP bridging.

Pump thrombosis, driveline infection, gastro-intestinal bleeding, and heart transplant within 1-year from d-LVAD implant were also similar regardless of stroke status (Table 4).

4 | DISCUSSION

The aim of this study was to investigate the incidence of post-d-LVAD stroke among patients requiring micro-axial flow-pump support as a bridge to d-LVAD therapy with a focus on the comprehensive tMCS strategy and pre-operative clinical course. The main results of this study can be summarized as follows:

1. The incidence of post-d-LVAD early ischemic stroke was 10.8%, while that of early hemorrhagic stroke was 2.9%.
2. Ischemic stroke, while associated with patient-related factors, did not appear to be modulated by the tMCS strategy and the pre-operative course.
3. Hemorrhagic stroke was associated with both patient-related factors and several factors related to the tMCS bundle of care, representing potentially actionable treatment targets.
4. Both early ischemic and hemorrhagic strokes were associated with increased 1-year mortality.

This study addresses important gaps in our understanding of stroke risk in patients undergoing d-LVAD implantation with mAFP bridging. While previous research has explored neurological complications in the broader d-LVAD population, the predictors, incidence, and consequences of stroke events among d-LVAD patients bridged

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 3 Univariate predictors of ischemic and hemorrhagic stroke occurrence among patients undergoing d-LVAD with mAFP bridging.

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	***p*-value**	**HR (95% CI)**	***p*-value**
Ischemic stroke				
Prior stroke (%)	2.34 (1.01–5.40)	**0.047**	–	–
mPAP (mm Hg)	1.03 (1.01–1.04)	**0.005**	–	–
Anemia (Hb <8 g/dL)	2.36 (1.02–5.43)	**0.044**	2.4 (1.1–5.5)	**0.047**
Hemorrhagic stroke				
Male sex	0.15 (0.04–0.55)	**0.004**		
BMI (kg/m^2)	1.11 (1.01–1.21)	**0.024**		
Cardiac arrest prior to mAFP implant	8.41 (1.75–40.47)	**0.008**		
mAFP 2.5/CP (vs. 5.0/5.5)	5.62 (1.41–22.71)	**0.015**	5.5 (1.1–27.8)	**0.039**
Hemolysis on mAFP support	10.49 (1.29–85.29)	**0.028**	–	–
Severe thrombocytopenia on mAFP support	5.30 (1.07–26.26)	**0.041**		
Renal replacement therapy on mAFP support	5.10 (1.27–20.37)	**0.021**		
ECMO support at LVAD implant	5.03 (1.35–18.72)	**0.016**	–	–
RBC transfusion post-LVAD implant (units)	1.11 (1.02–1.20)	**0.012**		

Abbreviations: Hb, hemoglobin; RBC, red blood cells; other abbreviations as in Table 1.

Bold values indicates level of significance was set at $p<0.05$

with mAFP had remained unclear. mAFP devices may heighten stroke (both ischemic and hemorrhagic) risk through several mechanisms including mechanical triggers, hemorheological alterations (high shear stress–induced acquired von Willebrand syndrome and platelet depletion), anticoagulation requirement, and blood products transfusions.[15] While these factors increase the stroke risk on mAFP support, they might conceivably have an impact on post-d-LVAD events as well. Moreover, the factors constituting the comprehensive tMCS management strategy including pump model, support duration, sequential and/or combined tMCS use and complications while on support might themselves modulate the stroke risk. We thus designed this study to shed light on the associations between various patient and management factors and the risk of early strokes in this complex setting, analyzing a large contemporary cohort of mAFP-bridged patients.

The findings of this study underscore several clinically relevant points. First, the occurrence of early ischemic and hemorrhagic strokes in patients undergoing d-LVAD implantation with mAFP bridging is not negligible. In the unselected INTERMACS cohort, the risk of early stroke was 6%.[1] Despite no formal statistical comparisons can be made, the nominally higher rates of early stroke observed in our cohort of patients undergoing d-LVAD implant with mAFP bridge suggests a direct relationship between the complexity of this higher-risk population, including the critical disease features and the pre-procedural management aspects, with the incidence of early stroke.[16] Importantly, despite increased risk in both ischemic and hemorrhagic strokes, the tMCS management strategy itself seems to exert a differential impact on ischemic and hemorrhagic events. Specifically, while several patient-related factors were associated with ischemic stroke, the tMCS strategy and complications did not seem to modulate its risk. Ischemic stroke was linked to a history of prior stroke, severe anemia, and higher mean pulmonary artery pressures before d-LVAD implantation. These associations may highlight the need for careful patient selection, closer monitoring, and optimization of pre-implantation conditions to reduce the risk of ischemic strokes.

Hemorrhagic stroke, on the other hand, exhibited a different set of risk factors. Patient-related factors such as female sex, body mass index, and cardiac arrest prior to mAFP implant were associated with an increased risk of hemorrhagic stroke. Additionally, factors related to the tMCS strategy and management, including the type of mAFP device, hemolysis, and ECMELLA at d-LVAD implant seems to modulate the risk of hemorrhagic stroke. These results are plausible and grounded on a solid pathophysiological rationale.

Regarding mAFP model, the pump hemocompatibility profile is directly related to the device-induced shear stress on the blood, that is, in turn related to rotational speed.[17–19] mAFP 2.5/CP as compared to 5.0/5.5 devices necessitate higher rotational speed per-flow generated, resulting in higher hemocompatibility-related complications. Of note, the higher pump position instability carried by mAFP 2.5/CP

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

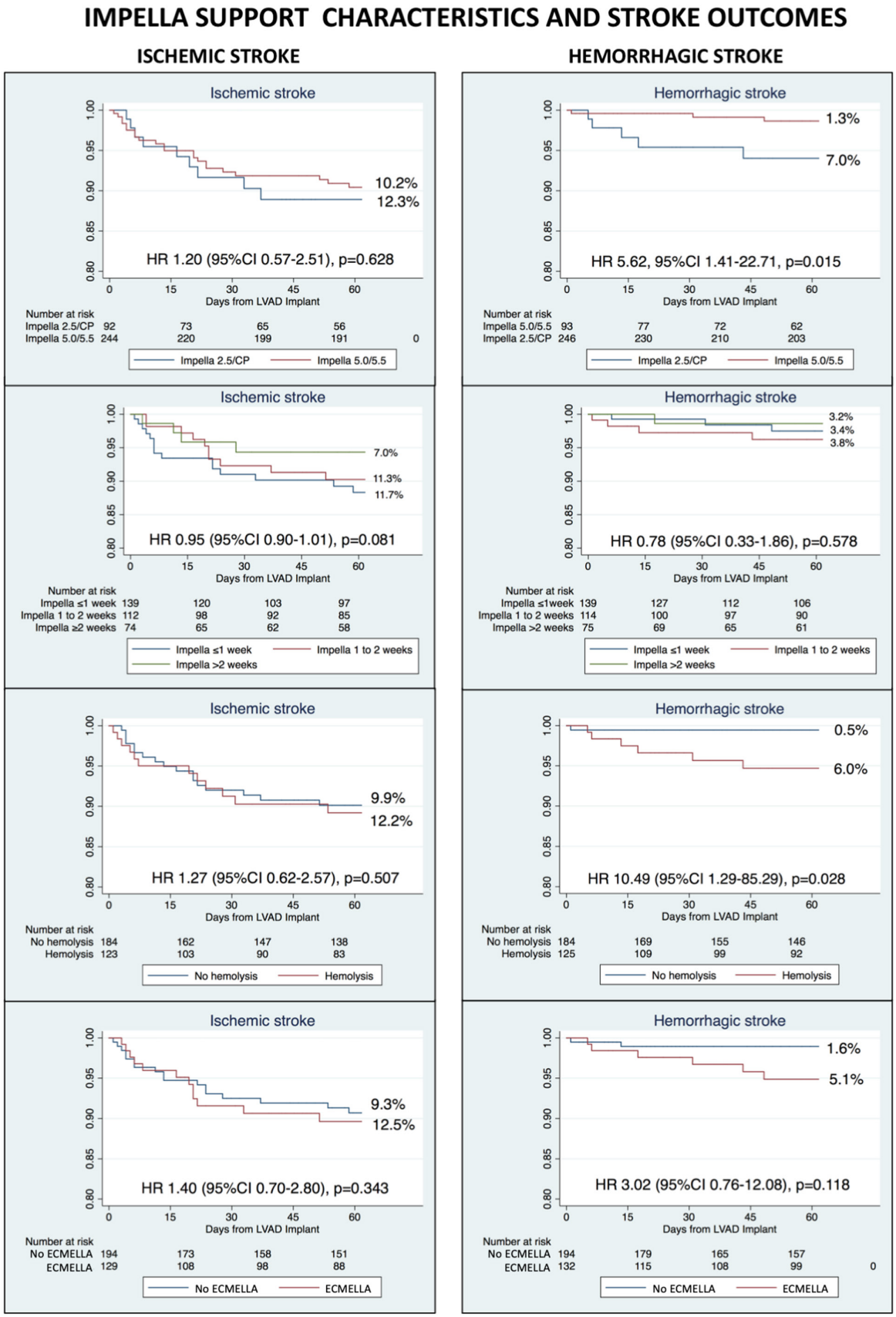

FIGURE 3 Kaplan–Meier estimates and hazard ratio for the association of selected mAFP support characteristics with early ischemic and hemorrhagic stroke following d-LVAD implant.

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 4 Association of ischemic and hemorrhagic stroke with d-LVAD-specific outcomes among mAFP-bridged patients.

	Ischemic stroke		Hemorrhagic stroke	
	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
All-cause death	2.67 (1.58–4.53)	**<0.001**	3.43 (1.49–7.88)	**0.004**
Heart transplant	3.29 (0.94–11.05)	0.062	5.26 (0.69–40.25)	0.109
Early severe RV failure	0.78 (0.31–1.97)	0.602	3.11 (0.81–11.88)	0.098
Pump thrombosis	0.04 (0.01–1722)	0.562	0.048 (0.01–30 897)	0.766
GI bleeding	2.94 (0.97–5.62)	0.059	2.64 (0.63–11.02)	0.184
Driveline infection	1.97 (0.84–4.63)	0.120	0.05 (0.01–696)	0.535

Abbreviations: GI, gastro-intestinal. Other abbreviations as in Table 1.

Bold values indicates level of significance was set at $p<0.05$

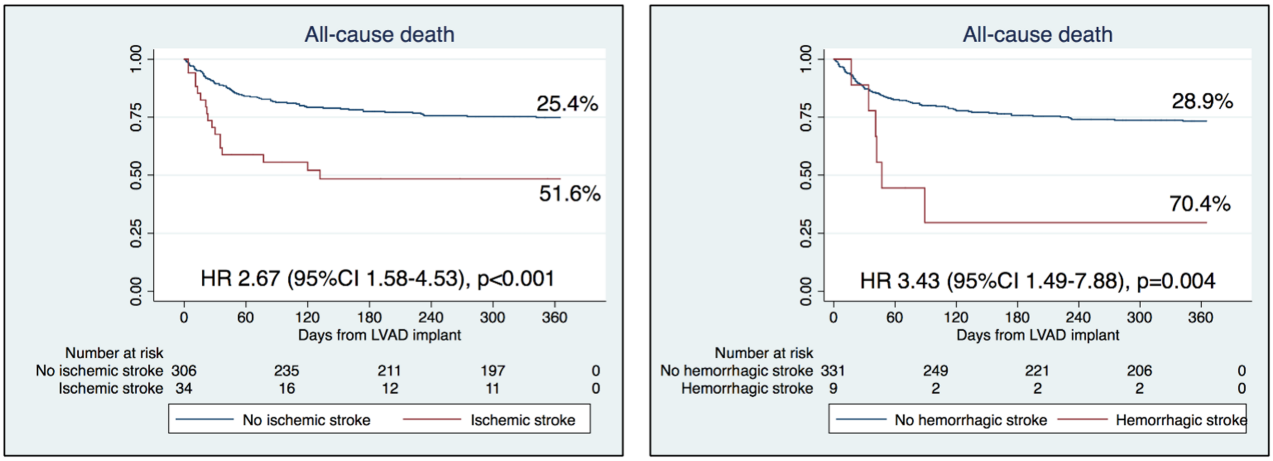

FIGURE 4 Kaplan–Meier estimates and hazard ratio for the association of early ischemic and hemorrhagic stroke with 1-year all-cause mortality on d-LVAD support.

might itself further contribute.[20,21] These concepts are substantiated by the higher hemolysis rate with mAFP 2.5/CP versus 5.0/5.5 observed in the present analysis. The relationship among mAFP model, hemolysis on support, and post-d-LVAD bleeding is likely complex and multifactorial. During critical illness, a precarious hemostatic balance is further exacerbated by the direct tMCS activation of the coagulation contact pathway, by the tMCS requirement for anticoagulation, and by blood product transfusions.[15,19] Of note, high shear stress–induced acquired von Willebrand syndrome and platelet depletion might represent one of the pathophysiological links between pump type, hemolysis, and post-d-LVAD hemorrhagic stroke.[15,19] Thus, the results of our study call for aggressive prevention and management of on-support hemolysis, and for further dedicated research on this topic.

ECMELLA at d-LVAD implant was associated with a 5-fold risk of post-d-LVAD hemorrhagic stroke. While persistent ECMELLA support at d-LVAD implant may identify a subgroup of patients at higher risk, it also implies higher management and procedural complexity that may itself play a role in post-d-LVAD hemorrhagic stroke. Accordingly, it remains pivotal to assess and to strive for tMCS de-escalation prior to d-LVAD implant in order to improve early procedural outcomes.[7]

Finally, beyond underscoring the multifactorial nature of hemorrhagic strokes in d-LVAD patients bridged with tMCS, and identifying several potential management targets, our results call for an individualized approach: patients at higher risk, including women, heavier patients, and post-cardiac arrest patients, might benefit from the use of more hemocompatible mAFP iterations, more aggressive hemolysis management and, potentially, more conservative anticoagulation targets.[22]

To summarize, early ischemic and hemorrhagic stroke events were associated with 2.7- and 3.4-fold mortality increase at 1 year, respectively, and the higher relative risk following hemorrhagic stroke as compared to ischemic stroke is also consistent with prior literature in the overall d-LVAD population and in patients bridged with ECMO.[16,23,24] These figures once again reinforce the ominous consequences of early stroke outcomes and underscore the need for continuous research to mitigate its incidence.

4.1 | Limitations

The results of the study should be interpreted considering several limitations. First, this study is hypothesis

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

generating and associative in nature. Moreover, while it identifies relationships between certain factors and stroke risk, it cannot establish causation. This notwithstanding, several associations highlighted in the study present clinical plausibility and call for addressing causation in dedicated studies. Second, the retrospective design may introduce bias, and practice variations among different institutions may influence outcomes. Third, the sample size, although substantial, may still limit the ability to detect some associations in relation to the low primary outcome rates, further precluding multivariate adjustment.

5 | CONCLUSIONS

In conclusion, among patients undergoing d-LVAD implantation with micro-axial flow-pump bridge, early ischemic and hemorrhagic strokes after d-LVAD implantation occur in a non-negligible proportion of patients. Early ischemic stroke, while associated with patient-related factors, did not appear to be modulated by the tMCS strategy and the pre-operative course. Conversely, hemorrhagic stroke was associated with several factors related to the tMCS bundle of care, representing potentially actionable treatment targets. Both early ischemic and hemorrhagic strokes were associated with increased 1-year mortality, highlighting the ominous consequence of these outcomes.

AUTHOR CONTRIBUTIONS

D.L. and E.V.P. designed the study and collected the data. G.G. performed the statistical analysis. G.G., D.L., and A.L. drafted the manuscript. All authors contributed significantly to the writing and critical review of the manuscript and approved the final draft.

CONFLICT OF INTEREST STATEMENT

JB has received honoraria and served as a consultant for Abiomed, Getinge, Resuscitec and Xenios. PL has received honoraria from Abiomed Inc and Abbott GmbH. The other Authors have no conflict of interest to report.

AFFILIATIONS

[1]City of Health and Science Hospital, Division of Cardiology, Department of Medical Sciences, University of Turin, Turin, Italy
[2]Department of Cardiothoracic and Vascular Surgery, Deutsches Herzzentrum der Charité (DHZC), Berlin, Germany
[3]Department of Cardiovascular Surgery, Charité—Universitätsmedizin Berlin, Berlin, Germany
[4]Heart and Diabetes Center, North Rhine-Westphalia, Bad Oeynhausen, Germany
[5]Department of Cardiovascular Surgery, University Heart Center Hamburg, Hamburg, Germany
[6]Department of Cardiac Surgery, Schüchtermann Clinic, Bad Rothenfelde, Germany
[7]Department of Cardiac Surgery, Heidelberg University Hospital, Heidelberg, Germany
[8]Institute of Clinical and Experimental Medicine, Prague, Czech Republic
[9]Department of Cardiac Surgery, University Hospitals Leuven, Leuven, Belgium
[10]Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, Milan, Italy
[11]Department of Cardiology, University Medical Center Utrecht, Utrecht, the Netherlands
[12]Department of Cardiothoracic Surgery, Rigshospitalet, Copenhagen, Denmark
[13]Department of Cardiovascular Surgery, University Hospital Duesseldorf, Duesseldorf, Germany
[14]Department of Cardiac Surgery, Leipzig Heart Center, Leipzig, Germany
[15]Department of Cardiothoracic Surgery, University Hospital Cologne, Cologne, Germany
[16]Department of Cardiac Surgery, University of Essen, Essen, Germany
[17]Department of Cardiothoracic Surgery, Jena University Hospital, Jena, Germany
[18]Department of Cardiac and Vascular Surgery, University of Mainz, Mainz, Germany
[19]Department of Cardiovascular Surgery, University Hospital Schleswig-Holstein, Kiel, Germany
[20]Department of Surgery, Division of Cardiac Surgery, Medical University of Vienna, Vienna, Austria
[21]DZHK (German Centre for Cardiovascular Research), partner site Berlin, Berlin, Germany
[22]City of Health and Science Hospital, Cardiac Surgery University Unit, Department of Surgical Sciences, University of Turin, Turin, Italy
[23]Second Department of Internal Medicine, Cardiovascular Medicine, General Teaching Hospital and 1st Faculty of Medicine, Charles University, Prague, Czech Republic
[24]Institute of Heart Diseases, Wroclaw Medical University, Wroclaw, Poland

ORCID

Guglielmo Gallone https://orcid.org/0000-0001-8011-6844
Daniel Lewin https://orcid.org/0000-0001-9831-6289
Ihor Krasivskyi https://orcid.org/0000-0003-0573-8218
Antonio Spitaleri https://orcid.org/0000-0002-4410-6232
Ilija Djordjevic https://orcid.org/0000-0002-5810-8626
Antonio Loforte https://orcid.org/0000-0002-3689-0477

REFERENCES

1. Yuzefpolskaya M, Schroeder SE, Houston BA, Robinson MR, Gosev I, Reyentovich A, et al. The Society of Thoracic Surgeons Intermacs 2022 annual report: focus on the 2018 Heart Transplant Allocation System The 13th annual report from The Society of Thoracic Surgeons (STS) Interagency Registry for Mechanically Assisted Cir. Ann Thorac Surg. 2023;115:311–39.
2. Tedford RJ, Leacche M, Lorts A, Drakos SG, Pagani FD, Cowger J. Durable mechanical circulatory support: JACC scientific statement. J Am Coll Cardiol. 2023;82:1464–81.
3. Teuteberg JJ, Cleveland JC, Cowger J, Higgins RS, Goldstein DJ, Keebler M, et al. The Society of Thoracic Surgeons Intermacs 2019 annual report: the changing landscape of devices and indications. Ann Thorac Surg. 2020 Mar 1;109(3):649–60.

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

4. Hernandez-Montfort JA, Xie R, Ton VK, Meyns B, Nakatani T, Yanase M, et al. Longitudinal impact of temporary mechanical circulatory support on durable ventricular assist device outcomes: an IMACS registry propensity matched analysis. J Heart Lung Transplant. 2020 Feb 1;39(2):145–56.
5. Akin S, Soliman O, de By TMMH, Muslem R, Tijssen JGP, Schoenrath F, et al. Causes and predictors of early mortality in patients treated with left ventricular assist device implantation in the European registry of mechanical circulatory support (EUROMACS). Intensive Care Med. 2020 Jul 1;46(7):1349–60.
6. Vallabhajosyula S, Arora S, Lahewala S, Kumar V, Shantha GPS, Jentzer JC, et al. Temporary mechanical circulatory support for refractory cardiogenic shock before left ventricular assist device surgery. J Am Heart Assoc. 2018 Nov 1;7(22):e010193.
7. Bertoldi LF, Pappalardo F, Lubos E, Grahn H, Rybczinski M, Barten MJ, et al. Bridging INTERMACS 1 patients from VA-ECMO to LVAD via Impella 5.0: de-escalate and ambulate. J Crit Care. 2020 Jun 1;57:259–63.
8. Bernhardt AM, Zipfel S, Reiter B, Hakmi S, Castro L, Söffker G, et al. Impella 5.0 therapy as a bridge-to-decision option for patients on extracorporeal life support with unclear neurological outcomes. Eur J Cardiothorac Surg. 2019 Dec 1;56(6):1031–6.
9. Cheng R, Tank R, Ramzy D, Azarbal B, Chung J, Esmailian F, et al. Clinical outcomes of Impella microaxial devices used to salvage cardiogenic shock as a bridge to durable circulatory support or cardiac transplantation. ASAIO J. 2019 Sep 1;65(7):642–8.
10. Willey JZ, Gavalas MV, Trinh PN, Yuzefpolskaya M, Reshad Garan A, Levin AP, et al. Outcomes after stroke complicating left ventricular assist device. J Heart Lung Transplant. 2016 Aug 1;35(8):1003–9.
11. Cowger JA, Shah P, Pagani FD, Grafton G, Stulak J, Chamogeorgakis T, et al. Outcomes based on blood pressure in patients on continuous flow left ventricular assist device support: an interagency registry for mechanically assisted circulatory support analysis. J Heart Lung Transplant. 2020 May 1;39(5):441–53.
12. Shah P, Birk SE, Cooper LB, Psotka MA, Kirklin JK, Barnett SD, et al. Stroke and death risk in ventricular assist device patients varies by ISHLT infection category: an INTERMACS analysis. J Heart Lung Transplant. 2019 Jul 1;38(7):721–30.
13. Amin AP, Spertus JA, Curtis JP, Desai N, Masoudi FA, Bach RG, et al. The evolving landscape of Impella use in the United States among patients undergoing percutaneous coronary intervention with mechanical circulatory support. Circulation. 2020;141:273–84.
14. Kormos RL, Antonides CFJ, Goldstein DJ, Cowger JA, Starling RC, Kirklin JK, et al. Updated definitions of adverse events for trials and registries of mechanical circulatory support: a consensus statement of the mechanical circulatory support academic research consortium. J Heart Lung Transplant. 2020;39:735–50.
15. Vandenbriele C, Arachchillage DJ, Frederiks P, Giustino G, Gorog DA, Gramegna M, et al. Anticoagulation for percutaneous ventricular assist device-supported cardiogenic shock: JACC review topic of the week. J Am Coll Cardiol. 2022;79:1949–62.
16. Saeed D, Loforte A, Morshuis M, Schibilsky D, Zimpfer D, Riebandt J, et al. Stroke complications in patients requiring durable mechanical circulatory support systems after extracorporeal life support. ASAIO J. 2023 Feb 1;69(2):145–50.
17. Esposito ML, Morine KJ, Annamalai SK, O'Kelly R, Aghili N, Pedicini R, et al. Increased plasma-free hemoglobin levels identify hemolysis in patients with cardiogenic shock and a trans valvular micro-axial flow pump. Artif Organs. 2019 Feb 1;43(2):125–31.
18. Jurmann MJ, Siniawski H, Erb M, Drews T, Hetzer R. Initial experience with miniature axial flow ventricular assist devices for postcardiotomy heart failure. Ann Thorac Surg. 2004 May;77(5):1642–7.
19. Van Edom CJ, Gramegna M, Baldetti L, Beneduce A, Castelein T, Dauwe D, et al. Management of bleeding and hemolysis during percutaneous microaxial flow pump support: a practical approach. JACC Cardiovasc Interv. 2023;16:1707–20.
20. Roberts N, Chandrasekaran U, Das S, Qi Z, Corbett S. Hemolysis associated with Impella heart pump positioning: in vitro hemolysis testing and computational fluid dynamics modeling. Int J Artif Organs. 2020 Nov 1;43(11):710–8.
21. Baldetti L, Beneduce A, Romagnolo D, Frias A, Gramegna M, Sacchi S, et al. Impella malrotation within the left ventricle is associated with adverse in-hospital outcomes in cardiogenic shock. JACC Cardiovasc Interv. 2023;16:739–41.
22. Baldetti L, Nardelli P, Ajello S, Melisurgo G, Calabrò MG, Pieri M, et al. Anti-thrombotic therapy with cangrelor and bivalirudin in venoarterial extracorporeal membrane oxygenation patients undergoing percutaneous coronary intervention: a single-center experience. ASAIO J. 2023 Jul 1;69(7):E346–E350.
23. Colombo PC, Mehra MR, Goldstein DJ, Estep JD, Salerno C, Jorde UP, et al. Comprehensive analysis of stroke in the long-term cohort of the MOMENTUM 3 study: a randomized controlled trial of the HeartMate 3 versus the HeartMate II cardiac pump. Circulation. 2019 Jan 8;139(2):155–68.
24. Acharya D, Loyaga-Rendon R, Morgan CJ, Sands KA, Pamboukian SV, Rajapreyar I, et al. INTERMACS analysis of stroke during support with continuous-flow left ventricular assist devices risk factors and outcomes. JACC Heart Fail. 2017;5(10):703–11.

How to cite this article: Gallone G, Lewin D, Rojas Hernandez S, Bernhardt A, Billion M, Meyer A, et al. Stroke outcomes following durable left ventricular assist device implant in patients bridged with micro-axial flow pump: Insights from a large registry. Artif Organs. 2024;00:1–12. https://doi.org/10.1111/aor.14775

15251594, 0, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/aor.14775 by Universita Di Torino, Wiley Online Library on [29/05/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License