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REPLY FROM AUTHORS: ATTEMPTING TO SOLVE THE PUZZLE—HOW TO UNVEIL THE TRUTH ABOUT THE ORIGIN OF STROKE IN POSTCARDIOTOMY EXTRACORPOREAL LIFE SUPPORT?

Reply to the Editor:

In our series of patients on postcardiotomy extracorporeal life support (ECLS), we described predominantly right hemispheric strokes in patients cannulated via the axillary artery. In accordance with our results, Grunfeld and colleagues[1] shared their experience and stress the role of primary procedure in the likelihood of developing ECLS-related stroke. Furthermore, they described a case of innominate artery occlusion in a patient with axillary artery ECLS cannulation recovering cardiac function, shifting interest on the flow phenomena in the watershed zone during weaning, and possible relation to stroke.

Because patients on postcardiotomy ECLS are an especially complex subset of cardiac surgical patients, there are various possible sources for stroke. Mechanisms can be divided into 3 possibilities: (1) Strokes taking place during the primary procedure. These strokes may be diagnosed during ECLS but are not attributable to ECLS. (2) Stroke related to embolism from an intracardiac source occurring during ECLS—with varying likelihood for intracardiac thrombus formation depending on primary procedure, and potentially cannulation site-related flow patterns. (3) Thromboembolism from the circuit and/or cannulation site—it remains difficult to clearly distinguish the origin of stroke; whereas in certain cases it may seem rather clear, in others it might not.

Ohira and colleagues[2] report an increased incidence of stroke associated with mitral valve replacement. We agree that the likelihood of intracardiac thrombus formation on ECLS is likely dependent on the primary procedure, and we included the primary procedure of all patients with stroke in our cohort in Table 1. It would be of interest whether, in the study by Ohira colleagues,[3] ECLS was prolonged in patients undergoing mitral valve replacement or whether the greater stroke rate was independent of longer support durations, and whether ECLS duration was included in the multivariable analysis. As there is obviously more time for intracardiac thrombus formation to occur with increasing ECLS duration, this may support that these patients should be weaned off ECLS as soon as possible.

A considerable issue in axillary cannulation seems to be right hemispheric stroke diagnosed shortly after ECLS explantation, suggesting thromboembolism from the cannulation site at the time of decannulation as the most likely mechanism. This is a mutual finding in our study[4] and the study of Ohira and colleagues,[3] who report 5 cases of stroke to right middle cerebral artery territory after decannulation in patients with axillary arterial cannulation. In our experience, in some patients, even thrombotic appositions in the circuit or even device stop were described in advance of catastrophic neurologic events. This leads to the conclusion that great care must be taken at the time of decannulation, especially after a long run duration, as thrombus formation at the site of cannulation may have occurred.

We further hypothesize that in cases of hemorrhagic stroke, small subclinical embolic lesions in the brain, caused by embolism from the ECLS circuit or cannulation site, in combination with ECLS-related flow alterations might be a mechanism of hemorrhagic stroke.

We feel this topic deserves further attention, and investigations of flow characteristics in the cerebral circulation depending on cannulation sites and flow rates and possible influence of cannulation site location on likelihood of stroke from an intracardiac origin are warranted.

TABLE 1. Characterization of all strokes (n = 48) with timing and clinical indication for CCT, preceding ECLS-related events, and possible causes, now including the type of initial surgery and preoperative left ventricular function

Cannulation site group	Patient #	Timing of CCT	Indication for CCT	Hemorrhagic/ ischemic	mRS score at discharge	Likely cause of stroke	Primary procedure	Preoperative LVEF
Axillary artery	1	Respiratory weaning/ after explant	Reduced vigilance	Hemorrhagic	1	Unknown	HTX	Preoperative LVAD
	2	Respiratory weaning/ after explant	Left-sided hemiplegia	Ischemic	4	ECLS	AVR + annular reconstruction (endocarditis)	45
	3	Respiratory weaning/ after explant	Left-sided hemiparesis	Ischemic	4	ECLS	Ascending aortic aneurysm repair + CABG	15
	4	Respiratory weaning/ after explant	coma	Hemorrhagic	6	ECLS	AVR + MV repair	15
	5	Directly after explant	Sudden-onset fixed dilated pupils	Hemorrhagic	6	ECLS explant	Bentall procedure	15
	6	2 days after explant	Left-sided hemiplegia, decrease of right-sided near-infrared spectroscopy to 29% directly after ECLS explant	Ischemic	4	ECLS explant	AVR + CABG + aortic arch repair	60
	7	Respiratory weaning/ after explant	Reduced vigilance	Ischemic	2	ECLS	AVR	25
	8	Respiratory weaning/ after explant	coma	Ischemic	4	ECLS	AVR + MV repair + CABG	25
	9	After extubation	Paresis of right arm	Ischemic	2	ECLS or surgery related (type A aortic dissection)	Aortic dissection repair (aortic arch replacement)	45
	10	2 weeks after ECLS explant, on regular ward before discharge	Visual field loss	Ischemic	1	Unknown/patient also had type A dissection	Aortic dissection repair (aortic reconstruction with patch + CABG)	60
	11	during ECLS run (day 6)	Sudden onset fixed dilated pupils on day 6 during ECLS run	Hemorrhagic	6	ECLS	HTX	Preoperative LVAD
	12	Respiratory weaning/ after explant	Reduced vigilance	Ischemic	1	Unknown, patient also underwent perioperative CPR	HTX	Preoperative LVAD
	13	Respiratory weaning/ after explant	Left-sided hemiplegia	Ischemic	4	Patient also had mechanical mitral valve thrombosis	MV replacement (thrombosed mechanical mitral valve)	40
	14	During ECLS run (day 3)	Sudden onset anisocoria at day 3 of ECLS	Ischemic	6	ECLS	AVR + MV – replacement + tricuspid valve repair + maze	30
	15			Ischemic	6		AVR + CABG	50

(Continued)

TABLE 1. Continued

Cannulation site group	Patient #	Timing of CCT	Indication for CCT	Hemorrhagic/ ischemic	mRS score at discharge	Likely cause of stroke	Primary procedure	Preoperative LVEF
		Respiratory weaning/ after explant	Coma, left-sided hemiplegia, embolectomy of right brachial artery after ECLS explant			ECLS related: CCT at beginning of ECLS normal, embolectomy right brachial artery after explant		
	16	Respiratory weaning/ after explant	Tetraparesis	Ischemic	5	ECLS	MV repair + tricuspid valve repair	25
	17	Respiratory weaning/ after explant	Tetraplegia and coma	Ischemic	6	Known left atrial thrombus and systemic embolism, also to left leg	AVR + MV replacement + CABG + MAZE	>50
	18	Respiratory weaning/ after explant	Unknown	Ischemic	3	Unknown	HTX	15
	19	Before hospital discharge	Visual field loss	Ischemic	1	Unknown, patient underwent concomitant right-sided carotid endarterectomy	AVR + CABG + carotid endarteriectomy	73
	20	During ECLS run (day 3)	Sudden onset fixed dilated pupils at day 3 of ECLS	Hemorrhagic	6	On ECLS	MV repair + TV repair	60
	21	Respiratory weaning/ after explant	Hemiplegia	Ischemic	4	ECLS	AVR + myectomy + annular augmentation	60
	22	During ECLS run (day 4)	Sudden onset anisocoria on day 4 of ECLS	Hemorrhagic	6	On ECLS	Aortic dissection repair (Bentall procedure + aortic arch replacement)	55
	23	Respiratory weaning/ after explant	NCSE	Ischemic	5	Unknown, also underwent CPR	MV replacement + CABG	unknown
	24	Respiratory weaning/ after explant	Aphasia, left-sided Hemiparesis	Ischemic	3	ECLS explanted because of device thrombosis despite adequate anticoagulation	Aortic dissection repair (ascending aortic replacement + CABG)	Unknown
	25	Respiratory weaning/ after explant	hemiplegia	Ischemic	4	ECLS, arterial cannula was changed due to thrombus formation	MV repair + CABG	25
	26	During ECLS run	Seizure	Ischemic	2	ECLS	AVR+TV replacement + myectomy + LAA closure	60

(Continued)

TABLE 1. Continued

Cannulation site group	Patient #	Timing of CCT	Indication for CCT	Hemorrhagic/ ischemic	mRS score at discharge	Likely cause of stroke	Primary procedure	Preoperative LVEF
	27	Respiratory weaning/ after explant	Reduced vigilance	Ischemic	1	Unknown	AVR + aortic root replacement (Freestyle) + CABG	60
	28	Respiratory weaning/ after explant	Left-sided hemiplegia and dysphagia	Ischemic	4	Patient had normal CCT 2 days before ECLS explant, large right sided ischemic stroke in CCT 3 days after ECLS explant	MV repair + CABG	45
	29	After arterial cannula change (same day)	Sudden onset anisocoria after cannula exchange	Hemorrhagic	6	Normal CCT 2 days before explant, onset of anisocoria after arterial cannula change due to thrombus formation	Bentall procedure	45
	30	Respiratory weaning/ after explant	Myoclonia	Ischemic	5	Unknown, potentially ECLS related	AVR+MV repair	65
	31	Respiratory weaning/ after explant	Reduced vigilance, positive Babinski right side	Ischemic	4	ECLS	MV repair + TV repair + LAA closure	65
	32	Directly after explant	fixed dilated pupils after explant, thrombus in arterial cannula	Ischemic	6	2 days after explant, occlusion of the right internal carotid artery was diagnosed and patient underwent thrombectomy; however, patient developed a fatal stroke. Thrombotic material in the arterial cannula was noted at the time of explant	MV replacement + TV repair	60
	33	On ECLS (day 3)	Sudden onset fixed dilated pupils	Hemorrhagic	6	ECLS	AVR+CABG	45
	34	Respiratory weaning/ after explant	Coma	Ischemic	6	Unknown, 30 min CPR	MV repair + TV repair + CABG + LAA closure + maze	60
	35	During ECLS (day 5)	Seizure	Ischemic	1	ECLS	PV-replacement	60
	36	On ECLS (day 3), after revision for mediastinal bleeding	Sudden onset fixed dilated pupils	Hemorrhagic	6	Hypertensive phase during revision for bleeding; fixed unresponsive pupils after revision→CCT	HTX	Preoperative LVAD

(Continued)

TABLE 1. Continued

Cannulation site group	Patient #	Timing of CCT	Indication for CCT	Hemorrhagic/ ischemic	mRS score at discharge	Likely cause of stroke	Primary procedure	Preoperative LVEF
	37	Respiratory weaning/ after explant	Reduced vigilance and seizure	Ischemic	3	Unknown	HTX	Preoperative LVAD
	38	During ECLS run (day 24)	unknown	Ischemic	6	ECLS	Ventricular rupture repair	unknown
	39	Respiratory weaning/ after explant	Hemiparesis and aphasia after extubation	Ischemic	4	ECLS	MV repair + TV repair + LAA closure + maze	60
	40	During ECLS (day 17)	Seizures, dilated pupils	Hemorrhagic	6	ECLS	MV repair + CABG	15
	41	Respiratory weaning/ after explant	Unknown	ischemic	1	Unknown, also had aortic dissection	Aortic dissection repair (Bentall + aortic arch repair)	31-50
Femoral artery	1	Respiratory weaning/ after explant	Reduced vigilance	Ischemic	1	ECLS	AVR+CABG	25
	2	Respiratory weaning/ after explant	Reduced vigilance	Ischemic	4	Embolic? Patient also underwent CPR before implant	MV repair + CABG	55
	3	Respiratory weaning/ after explant	Unknown	Ischemic	1	Watershed infarct, CPR before implant	Chronic type a dissection repair (ascending aortic replacement)	60
	4	During ECLS run (day 6)	Anisocoria	Ischemic	6	On ECLS, cannulation site was changed from femoral to axillary artery 4 days before the event	CABG	55
	5	Respiratory weaning/ after explant	Hemiparesis	Ischemic	3	Unknown, perioperative CPR	CABG	16-30
	6	On ECLS (day 8)	Anisocoria during ECLS run	Ischemic	6	ECLS, cannulation site was changed from femoral to axillary artery on day 4 after implant	Bentall procedure	31-50
	7	On ECLS (day 7)	Evaluation for durable left ventricular assist device implantation	Ischemic	6	Mechanical mitral valve thrombosis	AVR+MV replacement	49

Table adopted from Table E6 of the original manuscript. *CCT*, Cerebral computed tomography; *ECLS*, extracorporeal life support; *mRS*, modified Rankin Scale; *LVEF*, left ventricular ejection fraction; *HTX*, heart transplantation; *LVAD*, left ventricular assist device; *AVR*, aortic valve replacement; *CABG*, coronary artery bypass grafting; *MV*, mitral valve; *CPR*, cardiopulmonary resuscitation; *TV*, tricuspid valve; *NCSE*, nonconvulsive status epilepticus; *PV*, pulmonary valve; *LAA*, left atrial appendage.

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