DIU Réanimation Cardiopathiés Congénitales

Assistances Circulatoires : Nouvelles Perspectives

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Aucun conflit d’intérêts à déclarer

Thèmes principaux

- Classification
- PediMACS, Paedi-EUROMACS
- Hémostase - Anticoagulation - Antiaggregation
- Hémorragie
- Jarvik
- Impella
- MCS et CHD
- Destination therapy
- Qualité de vie
- Conclusions

Classification

Table 1 Approved Temporary and Durable Devices Eligible for Entry Into PediMACS

PediMACS devices	
Durable	Temporary
AbioCor TAH,Abiomed, Inc.	Abiomed AB5000, Abiomed, Inc.
MicroMed Debakey VAD-Child, Micromed Technology, Inc.	Abiomed BVS 5000, Abiomed, Inc.
SynCardia, Syncardia Systems, Inc.	Impella 2.5, Abiomed, Inc.
HeartMate II LVAS, Thoratec Corporation	Impella 5.0, Abiomed, Inc.
HeartMate IP, Thoratec Corporation	Impella CF, Abiomed, Inc.
HeartMate VE,Thoratec Corporation	Tandem Heart, CardiacAssist, Inc.
HeartMate XVE, Thoratec Corporation	Thoratec CentriMag, Thoratec Corporation, Inc.
Thoratec IVAD, Thoratec Corporation	Thoratec PediMag, Thoratec Corporation, Inc.
Thoratec PVAD, Thoratec Corporation	Biomedicus, Medtronic Biomedicus, Inc.
HeartWare HVAD, HeartWare, Inc.	Jostra Rotaflow, Maquet Cardiovasuclar
NovaCor PC, HeartWare, Inc.	Revolution, Sorin Group
NovaCor PCq, HeartWare, Inc.	
Berlin Heart EXCOR Pediatric, Berlin Heart, Inc.	

Classification

Table 2 Pedimacs Devices and Classifications

Device Class	Device Brand
Paracorporeal Pulsatile	AbioMed AB5000, Berlin Heart EXCOR, Thoratec PVAD
Paracorporeal Continuous	Thoratec Centrimag, Thoratec Pedimag, Maquet Rotaflow, Sorin Revolution
Implantable Continuous	HeartWare HVAD, HeartMate II LVAS
Percutaneous	Abiomed Impella 2.5/5.0, Tandem Heart, Abiomed Impella CP
Total Artificial Heart	Syncardia Total Artificial Heart

Classification

	Description of device	
- Extracorporeal	Pump for device located outside of the body	ECMO, CPB, EXCOR
- Intracorporeal	Pump for device located with the body	HeartMate 3, HVAD, Jarvik
- Temporary	Device intended for limited duration of support (hours-days; 3 weeks ?)	Impella 2.5, Impella CP, ECMO
- Durable	Device with capability of support for months-years	HeartMate 3, HVAD, Jarvik
- Partial Support	Device provides less flow than complete cardiac output	Impella 2.5-5.0-CP
- Full Support	Device provides complete cardiac output	ECMO, EXCOR, INCOR, HeartMate 3, HVAD
- Dischargeable	Device does not require hospitalization for continued support	HeartMate 3, HVAD

Classification

	Type of Flow	
- Pulsatile	Device with flexible membranes that creates intermittent flow and a pulse	Total artificial heart, EXCOR
- Non pulsatile/ Continous flow	Device that provides constant blood flow	HeartMate 3, HVAD, Pedimag, RotaFlow, Jarvik
- Axial	Device with inlet and outflow in the same axis and flow produced by rotating impeller	HeartMate 3, Jarvik
- Centrifugal	Device with inlet perpendicular to outflow tracts. Flow produced by centrifugal force.	HeartMate 2, HVAD, RotaFlow

Classification

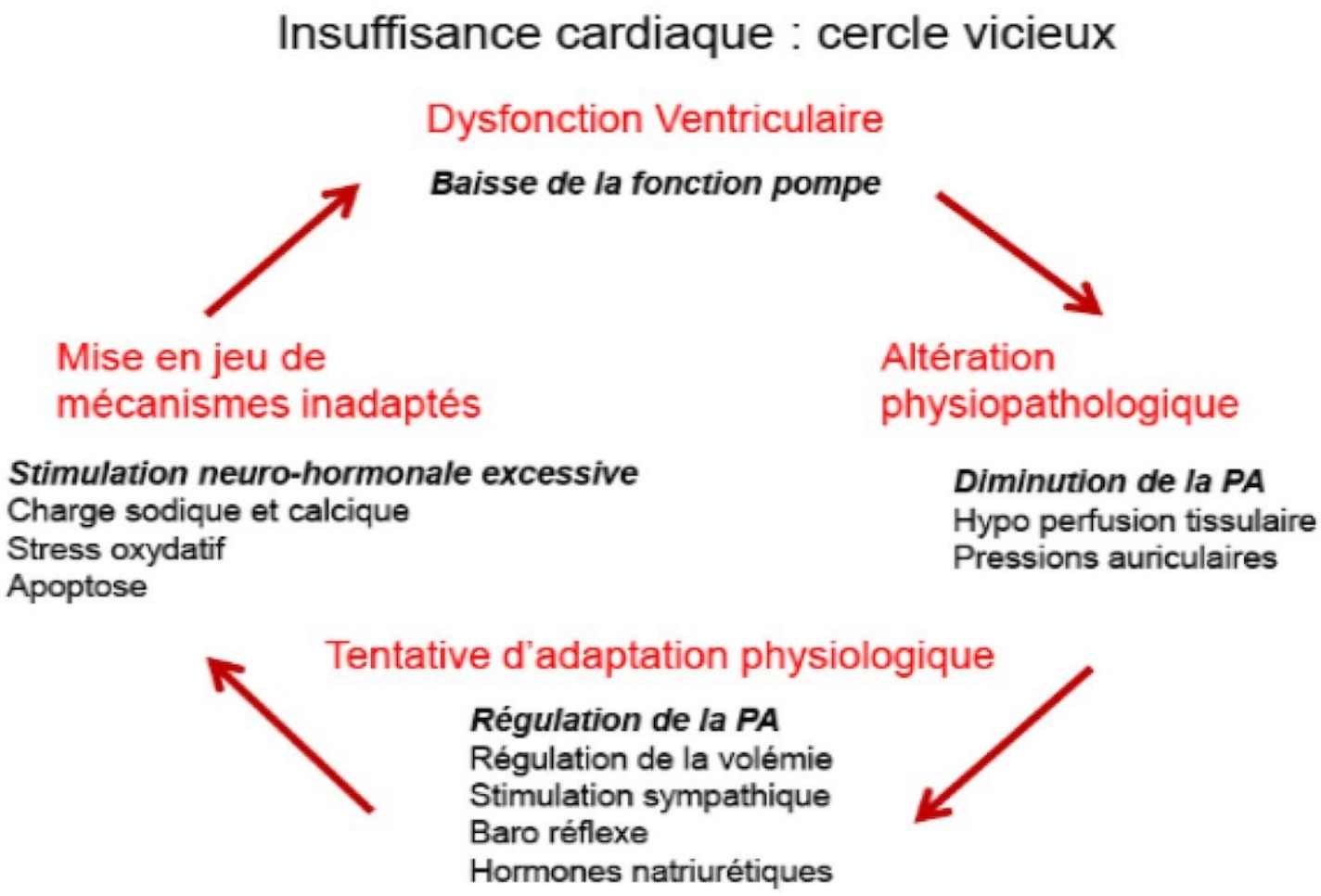
Indication for MCS use

- Bridge to transplant	Device implanted to support patient until a heart transplant	HeartMate II, HVAD
- Bridge to candidacy	Device implanted to support patient until can determine whether eligible for a heart transplant	HeartMate II, HVAD
- Bridge to recovery	Device implanted until myocardial recovery from injury	HeartMate II, HVAD
- Destination therapy	Device implanted to support patients who are ineligible for heart transplant	HeartMate II, HVAD, Jarvik
- Short term	New term to describe device implanted with intention for weeks-months of support (replaces bridge to transplant or recovery)	ECMO, Impella, Tandem, EXCOR
- Long term	New term to describe device implanted with the intention for years of support (replaces destination therapy)	HeartMate II, HVAD, Jarvik(?)

Long term MCS in CHD

Device	Manufacturer	Type of flow	Flows	Suggested BSA (m2)	Reference
Berlin Heart EXCOR®	Berlin Heart GmbH, Berlin, Germany	Pulsatile	10, 15, 25, 30, 50, and 60 mL (SV)	>0.7	Morales et. al (2011) Fraser et. al (2012) Almond, et al (2013) Weinstein et. al (2014) Conway, et al (2015) Morales, et al (2017)
HeartWare HVAD ®	Heart-Ware, Framingham, MA, USA	Continuous	2–10 L/min	> 1	Miera et. al (2011) Padalino et. al (2014) Sparks et al (2015) Stein et. al (2016) Miera et. al (2016) Imielskii et. al (2017) Pac, et al (2018
HeartMate II	Thoratec, Pleasanton, CA, USA	Continuous	0.5–10 L/min	>1.2	Owens et. al (2010) Morales et.al (2011) Cabrera et. al (2013) Lorts, et. al (2018)
HeartMate III	Thoratec, Pleasanton, CA, USA	Continuous	2.5–10 L/min	>1.2	
Total artificial Heart	Syncardia, Tucson, AZ, USA	Pulsatile	50cc and 70 cc (stroke volume)	> 1.7	Morales et. al (2012) Rossano et. al (2014) Adachi et. al (2014) Si et. al (2015) Ryan et. al (2015) Villa et. al (2017) Morales et. al (2017)
Jarvik 2000	Jarvik Heart,Inc., New York, NY, USA	Continuous	3–7 L/min	>1.2	Shah et. al, (2013)
Inf Jarvik 2015	Jarvik Heart, Inc., New York, NY, USA	Continuous	>1.2L/min	>0.4	Adachi, (2018)

Physiopathologie insuffisance cardiaque



INTERMACS

Interagency Registry for Mechanically Assisted Circulatory Support

PEDIMACS

Pediatric Interagency Registry for Mechanically Assisted Circulatory Support

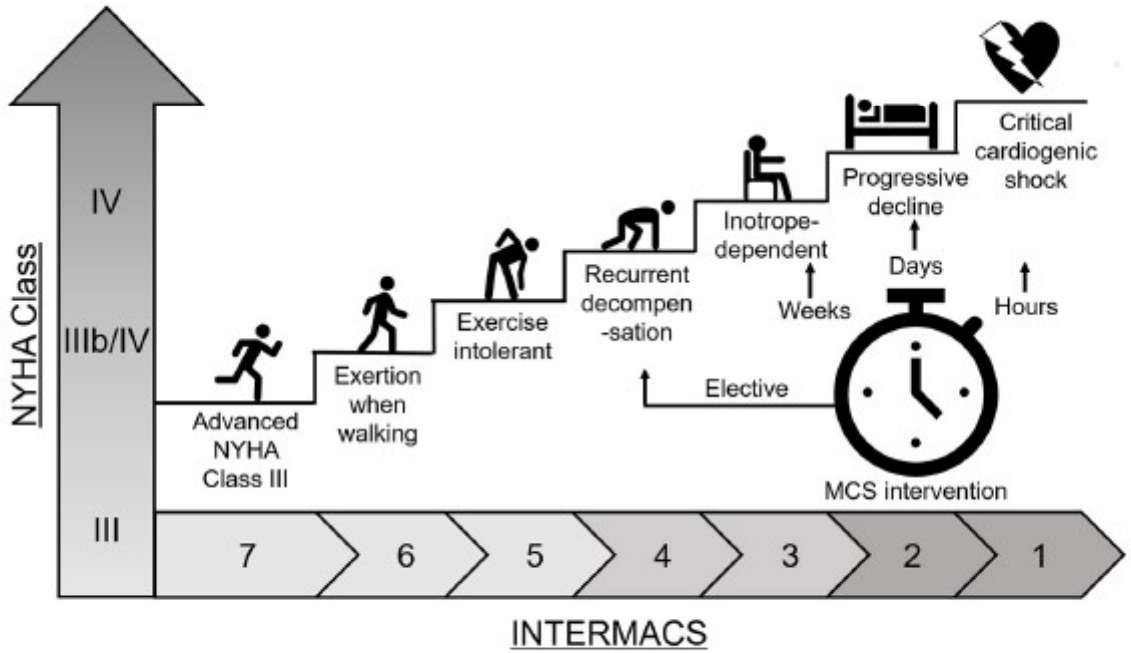


FIGURE 1 | Heart failure disease progression. Heart failure disease progression and INTERMACS profile for determination of patient treatment with mechanical circulatory support (MCS).

PEDIMACS

Outcomes of children implanted with ventricular assist devices in the United States: First analysis of the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS)

J Heart Lung Transplant. 2016 May;35(5):578-84

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- **1er registre Pédiatrique (Basé sur INTERMACS)**
- **< 19 ans, tous types de VAD, > 200 pt, 222 devices**
- **Multicentrique, rétrospective**
- **Sept 2012 - Juin 2015, 37 hôpitaux USA, statistique simple plutôt descriptive**

PEDIMACS

- **Classification** : durable – temporary
- **Profile des patients au moment de l'implantation du VAD** : âge, poids, diagnostique, CHD, previous cardiac surgery, INTERMACS,
≠ pulsatile devices **vs** continous implantables, previous ECMO
- **Device strategy :** LVAD, BiVAD, RVAD, TAH ; indications et suite (Transplantation, bridge to recovery, destination therapy)
- **Survival :** à 6 mois, différences selon profile INTERMACS
- **Causes/modes of death :** 19% ; MOF 39%, Neuro complic 14% ; 18% stop traitement
- **Competing outcomes :** greffe - survie on VAD - décès on VAD
- **Evénements indesirables :** 502 ; infections (Tardives), saignement/hémorragie (Précoces), problèmes sur le VAD, neuro ++

Blume ED, J Heart Lung Transplant. 2016

PEDIMACS

Objectifs du PediMACS

- Définir la meilleur stratégie de support pour enfants et ados

- Peaufiner la sélection des patients < 19 ans à soumettre à implantation de VAD

- Développer «les bonnes pratiques» par analyse des résultats

- Favoriser et guider développement et surveillance clinique des différentes type de VAD Ped et Adulte utilisés sur patientes < 19 ans

Blume ED, J Heart Lung Transplant. 2016

Second annual Pediatric Interagency Registry for Mechanical Circulatory Support (Pedimacs) report: Pre-implant characteristics and outcomes

Elizabeth D. Blume, MD,[a] Christina VanderPluym, MD,[a] Angela Lorts, MD,[b] J. Timothy Baldwin, PhD,[c] Joseph W. Rossano, MD,[d] David L.S. Morales, MD,[b] Ryan S. Cantor, MSPH,[e] Marissa A. Miller, DVM, MPH,[c] James D. St. Louis, MD,[f] Devin Koehl, BS,[e] David L. Sutcliffe, MD,[g] Pirooz Eghtesady, MD, PhD,[h] James K. Kirklin, MD,[e] and David N. Rosenthal, MD[i] for the Pedimacs Investigators

The Journal of Heart and Lung Transplantation, Vol 37, No 1, January 2018

- **Focus on caractéristiques pre-implantation. Outcomes et événements indésirables**
- **< 19 ans, 364 pt, 432 devices**
- **> 4 ans (Sept 2012-Sept 2016), 42 centres USA**

Table 1 Preimplant Characteristics of Pedimacs Patients (n=364)

Characteristic	Mean ± SD or No. (%)
Age, year	9.3 ± 6.5
Age group	
<1 year	69 (19.0)
1–6 years	66 (18.1)
6–10 years	56 (15.4)
11–19 years	173 (47.5)
Weight, kg	40.6 ± 33.0
Weight	
<5 kg	34 (9.4)
5-20 Kg	102 (28.1)
21-40 kg	68 (18.7)
41–70 kg	91 (25.1)
71–100 kg	49 (13.5)
>100 kg	19 (5.2)
Diagnosis	
Cardiomyopathy	223 (61.3)
Myocarditis	41 (11.3)
Congenital heart disease	77 (21.2)
Other	23 (6.3)
Non-white race	149 (40.9)
No previous cardiac operation	209 (57.4)
Heart failure before admission	206 (56.6)
AST > 100 U/liter	79 (22.6)
ALT > 100 U/liter	83 (23.6)
Creatinine > 1.6 mg/dl	17 (4.7)
Intubated	149 (49)
Inotropes	339 (93)
Paralyzed	69 (23)
TPN dependent	106 (35)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; Pedimacs, Pediatric Interagency Registry for Mechanical Circulatory Support; SD, standard deviation; TPN, total parenteral nutrition. The status of Intubated, Paralyzed, and TPN dependent were added to Pedimacs in protocol v4 and were available for 302 patients.

Blume ED J Heart Lung Transplant 2018

Table 4 Pre-Implant Patient Profile by Device Classification

Pre-implant patient profile[a]	Paracorporeal pulsatile No. (%)	Paracorporeal continuous No. (%)	Implantable continuous No. (%)
1: Critical cardiogenic shock	40 (38)	30 (51)	28 (16)
2: Progressive decline	56 (54)	25 (42)	110 (64)
3: Stable but inotrope dependent	6 (6)	4 (7)	26 (15)
4–7: Resting symptoms or less sick	2 (2)	...	8 (5)

[a]The pre-implant patient profile was missing for 6 patients.

Blume ED J Heart Lung Transplant 2018

PEDIMACS ≠ INTERMACS

- Les données sur les résultats ont été analysées par patient plutôt que par type d'appareil : certains patients pédiatriques prise en charge sur plusieurs types d'appareils (temporaires et durables) pendant toute la prise en charge
- *Echange d'appareils PAS une complication liée à l'appareil* (Comme dysfonctionnement ou thrombose pompe, typique des adultes). VADs pédiatrique : échange de dispositif lié à facteurs spécifiques du patient, associés aux changements dans les besoins physiologiques et hémodynamiques,
- PAS le reflet de l'efficacité du dispositif, mais plutôt la complexité en constante évolution des patients pédiatriques VAD
- Les résultats et les événements indésirables de Pedimacs : analyse de ces événements tout au long du parcours du patient assisté par le VAD, quel que soit le besoin d'une nouvelle pompe

Blume ED J Heart Lung Transplant 2018

Third Annual Pediatric Interagency Registry for Mechanical Circulatory Support (Pedimacs) Report: Preimplant Characteristics and Outcomes

Ann Thorac Surg
2019;107:993–1004

David L. S. Morales, MD, Joseph W. Rossano, MD, Christina VanderPluym, MD, Angela Lorts, MD, Ryan Cantor, PhD, James D. St. Louis, MD, Devin Koeh, BS, David L. Sutcliffe, MD, Iki Adachi, MD, James K. Kirklin, MD, David N. Rosenthal, MD, and Elizabeth D. Blume, MD, for the Pedimacs Investigators

- **< 19 ans, 423 pt, 508 devices , > 5 ans (Sept 2012-Sept 2016), 30 centres USA (Problèmes avec STS 1 Aout 2018 → >750 devices et > 600 patients PEDIMACS)**
- **Statistique plus complexe (Multivariate analysis)**
- **Pedimacs ≠ Intermacs**
- **Abordés les discours de la sortie à la maison (IC) et la qualité de vie**
- **Fc rénale eGFR et not**

Focus on résultats globaux + facteurs associés au risque de décès précoce, tardif et constant influencé par type de pompe et les différences correspondantes entre les cohortes des appareils, compris les données démographiques de leurs patients et les taux des événements indésirables

D Morales Ann Thorac Surg 2019

Table 2 Patient Characteristics Before Implant of a Durable Device

Baseline characteristics	All ($n = 200$)	Pulsatile flow ($n = 91$)	Continuous flow ($n = 109$)	p-value[a]
Age (y)	11 (0.03–18)	2 (0.03–17)	15 (0.64–18)	<0.0001
Age (y)				<0.0001
<1 year	31 (15.5)	30 (33.0)	1 (0.9)	
1 to 5 years	37 (18.5)	34 (37.4)	3 (2.8)	
6 to 10 years	31 (15.5)	14 (15.4)	17 (15.6)	
>10 years	101 (50.5)	13 (14.3)	88 (80.7)	
Weight (kg)	36 (3–141)	11.4 (3.0–135.0)	62.4 (15.5–141.0)	<0.0001
Weight (kg)				<0.0001
5 to 20 kg	59 (29.5)	55 (60.4)	4 (3.7)	
<5 kg	11 (5.5)	11 (12.1)		
>20 kg	130 (65.0)	25 (27.5)	105 (96.3)	
Female	78 (39.0)	42 (46.2)	36 (33.0)	0.0581
Cardiac diagnosis				0.0083
Cardiomyopathy	146 (73.0)	56 (61.5)	90 (82.6)	
Myocarditis	17 (8.5)	10 (11.0)	7 (6.4)	
Congenital heart disease	35 (17.5)	24 (26.4)	11 (10.1)	
Other	2 (1.0)	1 (1.1)	1 (0.9)	
Patient profile				0.0139
1. Critical cardiogenic shock	52 (27.1)	32 (36.8)	20 (19.0)	
2. Progressive decline	107 (55.7)	43 (49.4)	64 (61.0)	
3. Stable, but inotrope-dependent	25 (13.02)	7 (8.0)	18 (17.1)	
4. Resting symptoms or less sick	8 (4.2)	5 (5.7)	3 (2.9)	
Non-white race	80 (40.0)	35 (38.5)	45 (41.3)	0.6849
Previous cardiac operation	76 (38.0)	50 (54.9)	26 (23.9)	<0.0001
Previous ECMO	30 (15.0)	22 (24.2)	8 (7.3)	0.0009

Continuous variables are expressed as median (minimum-maximum). Categorical variables are expressed as number (%). ECMO, extracorporeal membrane oxygenation.

[a]Comparison of pulsatile- vs continuous-flow devices.

Pedimacs 1

Table 1 Preimplant Characteristics of Pedimacs Patients (n=364)

Characteristic	Mean ± SD or No. (%)
Age, year	9.3 ± 6.5
Age group	
<1 year	69 (19.0)
1–6 years	66 (18.1)
6–10 years	56 (15.4)
11–19 years	173 (47.5)
Weight, kg	40.6 ± 33.0
Weight	
<5 kg	34 (9.4)
5-20 Kg	102 (28.1)
21-40 kg	68 (18.7)
41–70 kg	91 (25.1)
71–100 kg	49 (13.5)
>100 kg	19 (5.2)
Diagnosis	
Cardiomyopathy	223 (61.3)
Myocarditis	41 (11.3)
Congenital heart disease	77 (21.2)
Other	23 (6.3)
Non-white race	149 (40.9)
No previous cardiac operation	209 (57.4)
Heart failure before admission	206 (56.6)
AST > 100 U/liter	79 (22.6)
ALT > 100 U/liter	83 (23.6)
Creatinine > 1.6 mg/dl	17 (4.7)
Intubated	149 (49)
Inotropes	339 (93)
Paralyzed	69 (23)
TPN dependent	106 (35)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; Pedimacs, Pediatric Interagency Registry for Mechanical Circulatory Support; SD, standard deviation; TPN, total parenteral nutrition. The status of Intubated, Paralyzed, and TPN dependent were added to Pedimacs in protocol v4 and were available for 302 patients.

Pedimacs 2

INCLUSION CRITERIA FOR MCS

1. NYHA IV (Ross IV pts 6 ans), insuffisance cardiaque réfractaire traitement médical, avec 1 des critères suivant :

a) INTERMACS 1 ou 1A: choc cardiogénique

b) INTERMACS 2 OU 2A : risque décès non immédiat moins < réponse inotropes ; dégradation à cause TDR + 1 des critères suivant :

* *dégradation fc rénale*
* *dégradation état nutritionnel*
* *dégradation mobilité, déambulation* secondaire à insuffisance cardiaque ou ses traitement (IOT → Bed rest)

c) ECMO ou Short-Term MCS

d) Pose CEC IMPOSSIBLE(CHD ; iscription liste greffe)

Pedimacs 2

INCLUSION CRITERIA FOR MCS

2. Inscription en liste
3. Circulation BiV, cardiomiopathie, CHD reparé (ALCAPA; Sténose Ao), cardiopathie acquise (Myocardite, Kawasaki)
4. Age 0-16 ANS ; âge gestationnel corrigé > 37 SA
5. Poids >/= 3 kgs e =/< 60 kgs
6. Tutelle parentale/légale (Et patient si âge appropriée), comprend la procédure et la prise en charge à long-terme, signature consentement écrit avant implantation

EXCLUSION CRITERIA FOR MCS

1. CIV apicale ou autres lésions à réparer
2. TIH, pathologies plaquettes ou contrindications AC/AG
3. Pathologie coagulation (Déficit FVIII, CIVD) ou thrombofilie (Mutation FV Leiden)
4. Maladies hématologiques → fragilité GR ou hémolyse
5. Infection récente (</=48H) avec Hémoc +/T > 38°C/↑ CRP/ Leucocytoses > 15x10*3/ml)
6. HIV, SIDA, Cancer
7. AVC < 30 jours, malformation SNC associée risque saignement (MAV, Moya-Moya)
8. Maladies psychiatriques, altérations du comportement (Antisociaux) avec risque de pas adhérer au traitement
9. Autre protocole investigation-Drug Trial non complétés ou follow-up non terminé

Pedimacs 2

Table 1. Characteristics of Pediatric Interagency Registry for Mechanical Circulatory Support Patients—Coverage: September 19, 2012, to December 31, 2017

Characteristics[a]	Overall (n = 423)	Paracorporeal Pulsatile (n = 121)	Paracorporeal Continuous (n = 79)	Implantable Continuous (n = 197)	*p* Value[b]	CHD Patients (n = 86)
Age, years	8.7 ± 6.4	3.3 ± 3.9	3.9 ± 5.2	13.4 ± 3.8	<0.0001	5.7 ± 5.8
Age group					<0.0001	
<1 year	89 (21)	52 (43.0)	37 (46.8)			29 (33.7)
1–5 years	79 (19)	46 (38.0)	23 (29.1)	9 (4.6)		22 (25.6)
6–10 years	71 (17)	13 (10.7)	7 (8.9)	44 (22.3)		17 (19.8)
11–19 years	184 (43)	10 (8.3)	12 (15.2)	144 (73.1)		18 (20.9)
Weight, kg	37.8 ± 32.1	13.9 ± 14.5	18.5 ± 20.8	57.2 ± 29.2	<0.0001	21.7 ± 23.5
Weight					<0.0001	
<5 kg	45 (11)	26 (21.5)	19 (24.4)			20 (23.3)
5–20 kg	119 (28)	71 (58.7)	37 (47.4)	10 (5.1)		35 (40.7)
21–40 kg	93 (22)	18 (14.9)	10 (12.8)	59 (29.9)		16 (18.6)
41–70 kg	96 (23)	5 (4.1)	9 (11.5)	71 (36.0)		11 (12.8)
71–100 kg	50 (12)		3 (3.8)	42 (21.3)		2 (2.3)
>100 kg	19 (5)	1 (0.8)		15 (7.6)		2 (2.3)
Diagnosis					<0.0001	
Cardiomyopathy	261 (62)	72 (59.5)	33 (41.8)	149 (75.6)		
Dilated	244 (93)	64 (88.9)	31 (93.9)	142 (95.3)		
Restrictive	11 (4)	6 (8.3)	1 (3.0)	4 (2.7)		
Hypertrophic	6 (2)	2 (2.8)	1 (3.0)	3 (2.0)		
Myocarditis	48 (11)	15 (12.4)	12 (15.2)	19 (9.6)		
Congenital heart disease	86 (20)	25 (20.7)	30 (38.0)	23 (11.7)		86 (100)
Single ventricle	52 (61)	15 (60.0)	22 (73.3)	13 (56.5)		52 (61)
Double ventricle	34 (40)	10 (40.0)	8 (26.7)	10 (43.5)		34 (40)
Other	28 (7)	9 (7.4)	4 (5.1)	6 (3.0)		
Patient profile					<0.0001	
1. Critical cardiogenic shock	138 (33)	49 (40.5)	38 (48.7)	38 (19.3)		34 (40.0)
2. Progressive decline	232 (55)	61 (50.4)	32 (41.0)	127 (64.5)		40 (47.1)
3. Stable but inotrope dependent	44 (11)	9 (7.4)	8 (10.3)	27 (13.7)		11 (12.9)
4–7. Resting symptoms or less sick	7 (2)	2 (1.7)		5 (2.5)		
Device type					<0.0001	
LVAD	342 (81)	88 (73.6)	54 (68.4)	180 (91.4)		66 (76.7)
RVAD	14 (3)	3 (2.5)	6 (7.6)	4 (2.0)		11 (12.8)
BiVAD	64 (15)	29 (24.0)	19 (24.1)	13 (6.6)		7 (8.1)
Total artificial heart	3 (1)	…	…	…		2 (2.3)
Device strategy					<0.0001	
Bridge to transplant-listed	231 (55)	96 (79.3)	33 (41.8)	95 (48.2)		52 (60.5)
Bridge to candidacy	146 (34)	23 (19.0)	24 (30.4)	94 (47.7)		22 (25.6)
Destination therapy	7 (2)	2 (1.7)		5 (2.5)		1 (1.2)
Bridge to recovery	25 (6)		18 (22.8)	2 (1.0)		7 (8.1)
Other	14 (3)		4 (5.1)	1 (0.5)		4 (4.7)
Previous cardiac operation	165 (39)	52 (43.0)	42 (53.2)	57 (28.9)	0.0003	76 (88)
ALT >100 U/L	102 (25)	29 (24.8)	17 (23.6)	49 (25.5)	1.0	15 (19)
Bilirubin >1.2 mg/dL	147 (40)	41 (35.7)	32 (52)	66 (39.3)	0.1	45 (62)
eGFR (mL · min^{-1} · 1.73 m^{-2})					0.0003	
<30	19 (5)	5 (4.2)	9 (12.0)	5 (2.6)		19 (22.6)
30–60	102 (25)	32 (27.1)	26 (34.7)	37 (19.1)		4 (4.8)
>60	291 (71)	81 (68.6)	40 (53.3)	152 (78.4)		61 (72.6)
Intubated	194 (45)	81 (77.1)	61 (85.9)	38 (21.0)	<0.0001	53 (69.7)
Inotropes	397 (94)	112 (92.6)	73 (93.6)	187 (94.9)	0.7	82 (95.3)
Paralyzed	101 (27)	44 (42.7)	31 (43.7)	17 (9.6)	<0.0001	30 (40.0)
Feeding tube/TPN dependent	232 (64)	92 (90.2)	61 (93.8)	66 (38.4)	<0.0001	59 (81.9)

[a] Data are presented as the mean ± SD or number (%). [b] The *p* value compares characteristics across the 3 device classifications.

ALT = alanine aminotransferase; BiVAD = biventricular assist device; CHD = congenital heart disease; eGFR = estimated glomerular filtration rate; LVAD = left ventricular assist device; RVAD = right ventricular assist device; TPN = total parental nutrition.

- **Age**
- **Poids**
- **Diagnostic**
- **Profile INTERMACS**
- **Type de pompe (G/D/B/TAH)**
- **Stratégie**
- **ATCD Chir Cardiaque**
- **ALT (foie)**
- **Bilirubine (Cholestase)**
- **eGFR /fc (rein)**
- **Intubation**
- **Inotropes**
- **Curarisation**
- **Nutrition**

Pedimacs 3

D Morales Ann Thorac Surg 2019;107:993–1004

- **Mortalité et EI ↔ Timing implantation et profile INTERMACS**

- **Durable VAD si profile 1 → outcome plus mauvais**

- **< poids et CHD mauvais pronostique vs CMD et enfants plus âgés**

- **Groupe IC moins « malade » plus âgé moins CHD VS groupe PC - PP**

- **PC ≈ PP mais PP plus CHD (>50%) état pré-implantation plus mauvais (Profile 1 50%, IH 52% et IR 47%) → Probablement indication/projet ≠ → 20% patients PC recovery dans 3 mois VS < 1% recovery pour IC-PP**

- **PC device : assistance temporaire de 1ere choix pour BRIDGE TO TRANPLANTATION population « haute risque » (VU, < 5 kgs, AntiCoagulation difficile) → > 30% greffés à 6 mois**

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VU < 5 kgs, LCOS ???

Pose canules Berlin-Heart EXCOR

ECMO V-A

- Récupération → Sevrage → Ablation canules et pompe
- PAS de récupération → Implantation device long durée → Mise en liste de greffe sans MOF

Pedimag, Centrimag, etc (pas oxygenateur)

- Récupération → Sevrage → Ablation canules et pompe
- PAS de récupération → Implantation device long durée → Mise en liste de greffe sans MOF

Evénements indésirables (EI)

- **Infection, saignement, complications neurologiques, dysfonctionnement du dispositif : > 60% MCS 1 ou plus; principalement < 3 mois ; 25% hémorragie majeure ou infection ; principalement PC**

- **≠ entre centres USA**

- **ACTION = Advanced Cardiac Therapies Improving Outcomes Network**

- **NEURO : AVC hémorragiques et ischémiques + convulsions, encéphalopathie, lésions radiologique asymptomatiques, état confusionnel, frontalisation, autisme, saignement extrassial**
  23% précoces et 5% tardifs, AVC 11% préc et 2% tard; IC < que PP/PC

- **AVC ischémiques > hémorragiques (Optimisation anticoagulation ? Amélioration surveillance ?) = rôle du réseau ACTION**

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Table 5. Adverse Events, Pediatric Interagency Registry for Mechanical Circulatory Support Pedimacs Patients (n = 423)—Coverage: September 19, 2012, to December 31, 2017

		Overall		Paracorporeal Pulsatile			Paracorporeal Continuous			Implantable Continuous		
Event	Period[a]	Patient Percent (%)	Rate[b]	Patient Percent (%)	Rate[b]	Device Incidence[c] (%)	Patient Percent (%)	Rate[b]	Device Incidence[c]	Patient Percent (%)	Rate[b]	Device Incidence[c] (%)
Bleeding	Early	27	2.7	25	1.9	27	38	6.5	30	23	1.9	28
	Late	5	0.3	3	0.4		1	0.4		8	0.2	
Infection	Early	24	2.2	23	2.3	26	28	4.4	24	22	1.6	30
	Late	9	0.7	8	1.2		3	1.3		13	0.6	
Device malfunction	Early	20	2.4	27	3.8	33	32	7.3	30	11	0.6	19
	Late	7	0.6	11	1.7		1	0.4		9	0.4	
Neurologic dysfunction	Early	23	1.8	27	2.3	33	37	4.6	29	15	0.9	18
	Late	5	0.3	6	0.6		3	0.9		6	0.2	
CVA	Early	11	0.8	18	1.3	19	13	1.4	10	8	0.5	10
	Late	2	0.1	3	0.2					4	0.1	
Ischemic stroke	Early	8	0.5	13	0.9	13	9	0.9	8	5	0.3	6
	Late	1	0.08	1	0.07					2	0.08	
Hemorrhagic stroke	Early	4	0.2	5	0.4	6	3	0.4	3	3	0.2	5
	Late	1	0.07	2	0.1					2	0.05	

[a] Early: within 3 months after implant; late: beyond 3 months after implant. [b] Rates are reported per patient-year. [c] Device incidence indicates overall percentage of patients within the device group experiencing the specified event.

CVA = cerebrovascular accident.

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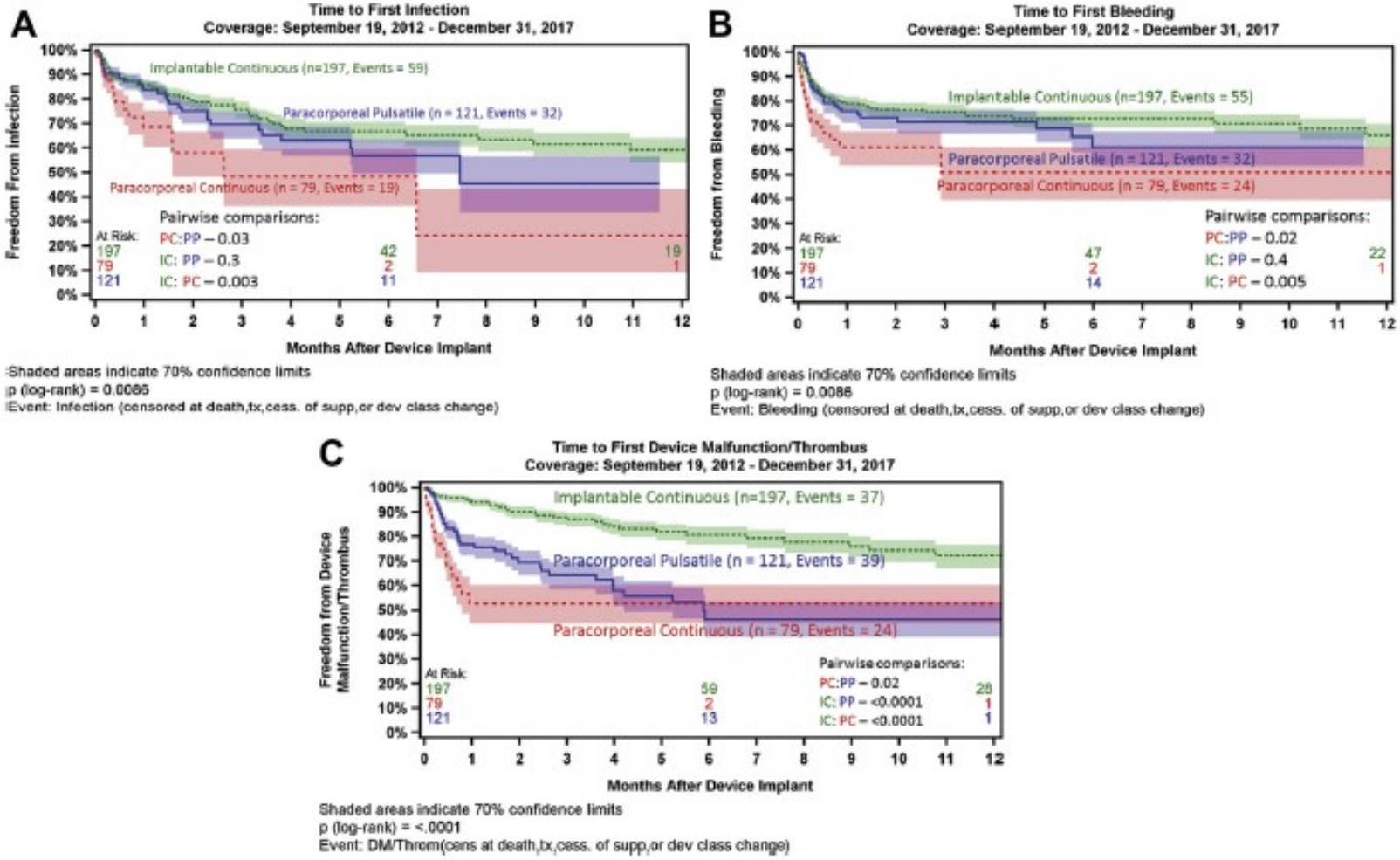

Fig 4. Kaplan-Meier depiction of freedom from (A) first infection, (B) major bleeding, and (C) device malfunction (DM) or thrombosis, stratified by device type. The shaded areas indicate the 70% confidence limit. (IC = implantable continuous; PC = paracorporeal continuous; PP = paracorporeal pulsatile.)

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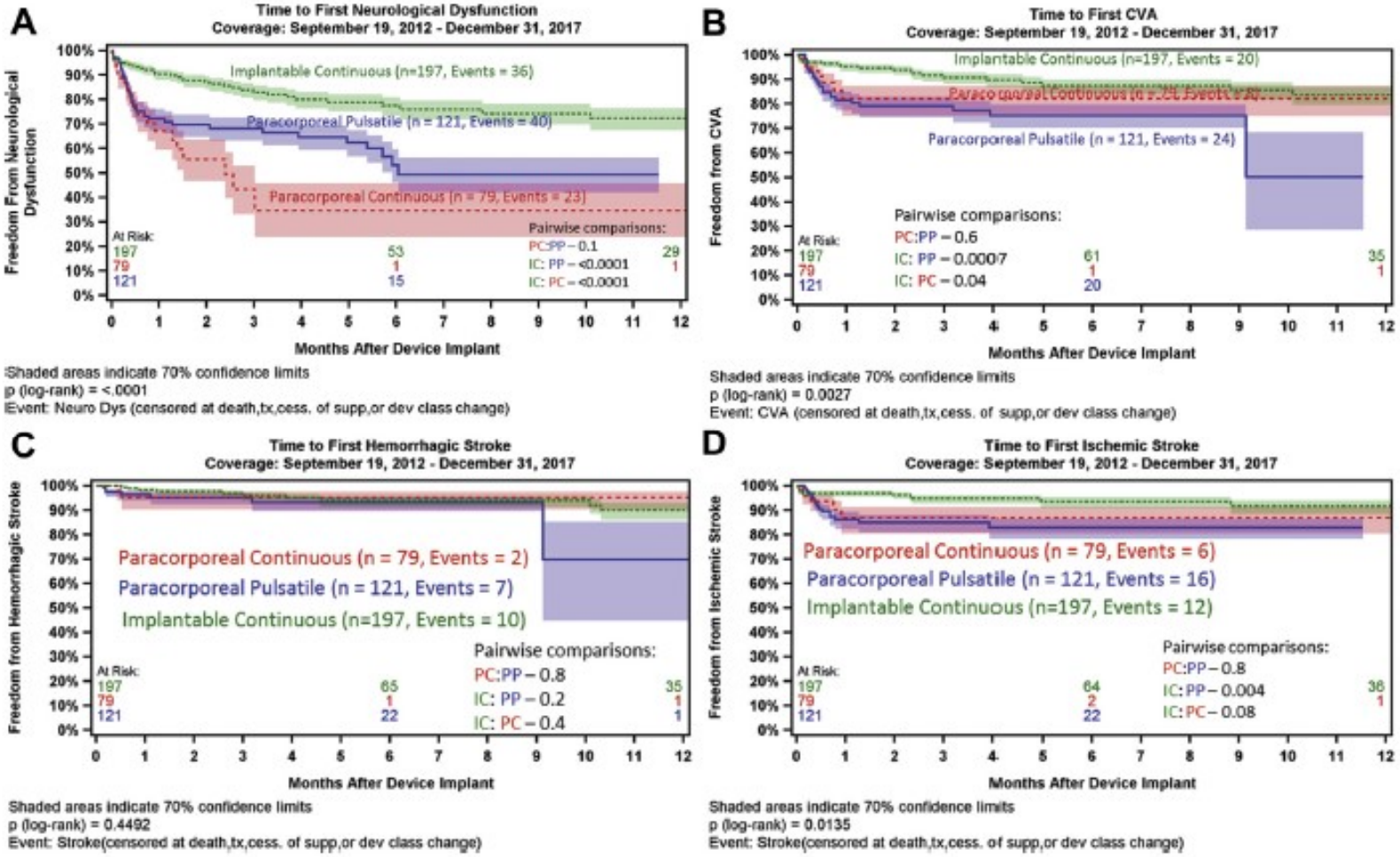

Fig 5. Kaplan-Meier depiction of freedom from (A) first neurologic event, (B) cerebrovascular accident (CVA), (C) hemorrhagic stroke, and (D) ischemic stroke, stratified by device (dev) type. The shaded areas indicate the 70% confidence limit. (cess. of supp = cessation of support; IC = implantable continuous; PC = paracorporeal continuous; PP = paracorporeal pulsatile; tx = transplantation.)

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Mortalité et outcomes

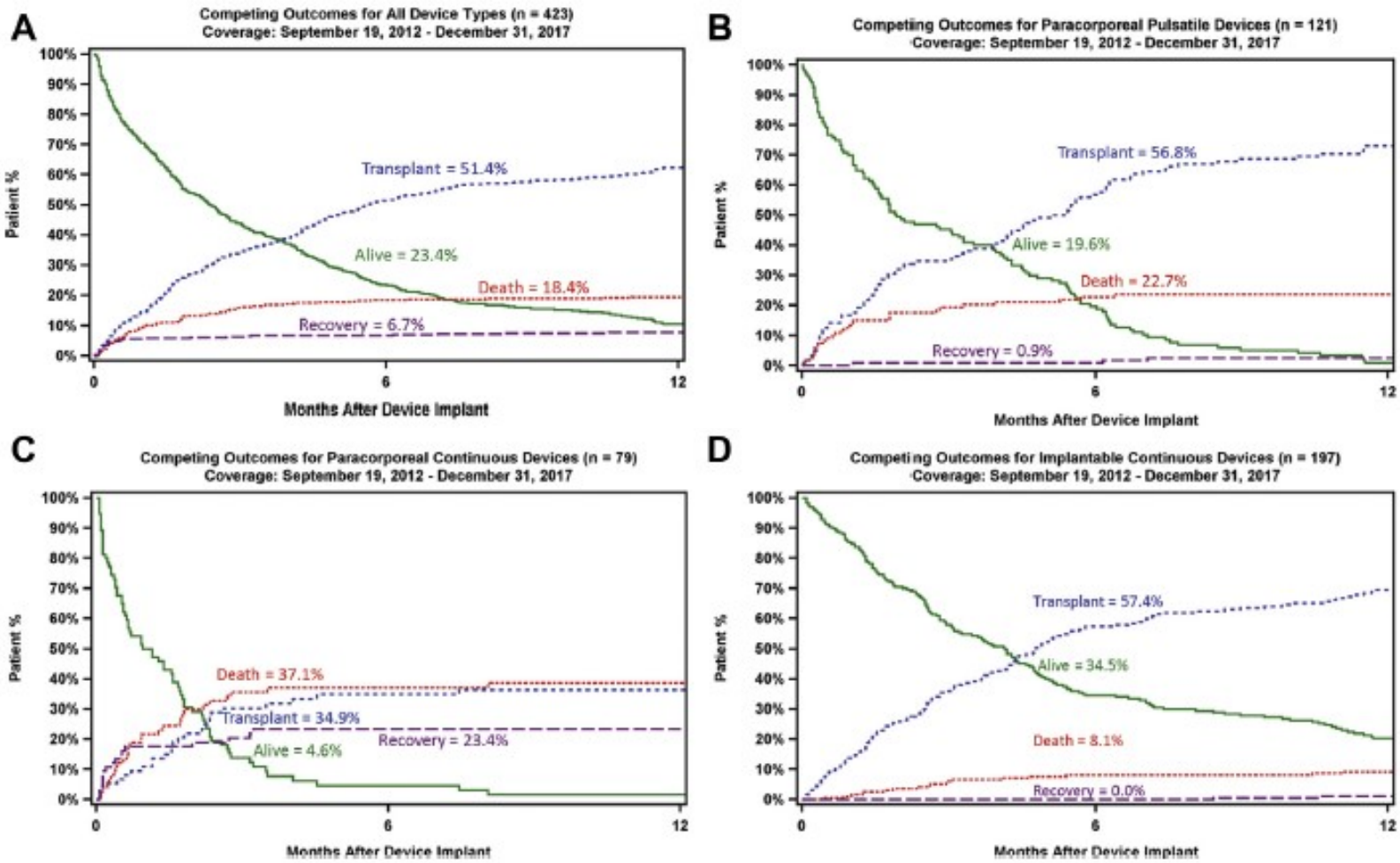

Fig 3. Competing outcomes depiction for patients receiving (A) any device type, (B) paracorporeal pulsatile-flow devices, (C) paracorporeal continuous-flow devices, or (D) implantable continuous-flow devices. At any time point, the sum of the proportions for the various outcome events (all mutually exclusive) equals 100%.

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Table 6. Parametric Hazard Modeling Overall, Pediatric Interagency Registry for Mechanical Circulatory Support Patients (n = 423)—Coverage: September 19, 2012, to December 31, 2017

	Early Hazard		Constant Hazard	
Risk Factors for Death	HR (95% CI)	*p* Value	HR (95% CI)	*p* Value
BiVAD	3.6 (1.8–7.3)	0.0004		
Patient profile 1	2.6 (1.4–5.0)	0.003		
Paracorporeal continuous device	4.1 (2.0–8.4)	0.0001		
Percutaneous device	13.5 (4.4–41.2)	<0.0001		
Small-volume center (<15 patients)	3.3 (1.8–6.4)	0.0002		
Severe right ventricular ejection fraction	0.4 (0.2–0.7)	0.002		
Weight (kg)	0.9 (0.9–1.0)	0.001		
Age squared (years)	1.01 (1.0–1.02)	0.02		
Functional capacity–intubated			4.3 (1.5–12.8)	0.008
Bilirubin (mg/dL)			1.1 (1.0–1.1)	0.02

BiVAD = biventricular assist device; CI = confidence interval; HR = hazard ratio.

Table 7. Parametric Hazard Modeling for Paracorporeal Pulsatile Devices, Pediatric Interagency Registry for Mechanical Circulatory Support Patients (n = 121)—Coverage: September 19, 2012, to December 31, 2017

	Early Hazard	
Risk Factors for Death	HR (95% CI)	*p* Value
Dialysis	23.2 (7.6–70.4)	<0.0001
Era September 2012 to 2014	2.6 (1.1–5.9)	0.03
Small-volume center (<15 patients)	4.4 (2.1–9.4)	0.0001
Natural log of age (years)	0.7 (0.5–0.8)	0.0005

CI = confidence interval; HR = hazard ratio.

Table 8. Parametric Hazard Modeling for Paracorporeal Continuous Devices, Pediatric Interagency Registry for Mechanical Circulatory Support Patients (n = 79)—Coverage: September 19, 2012, to December 31, 2017

	Early Hazard	
Risk Factors for Death	HR (95% CI)	*p* Value
Blood Type O	4.0 (1.2–13.3)	0.03
History of valve operation	8.5 (1.9–38.8)	0.006
Severe RVEF	2.8 (1.2–6.5)	0.01
AST (U/L)	1.0 (1.0–1.0)	0.001

AST = aspartate aminotransferase; CI = confidence interval; HR = hazard ratio; RVEF = right ventricular ejection fraction.

- **Outcomes dépendent de facteurs démographiques et gravité maladie pré-implantation**

- **Facteurs associés à mortalité : percutanée, BiVAD , centres avec moins de volume (< 15 VADs/année)**

- **IC-VAD : ECMO pré-implantation**

- **PP-VAD : gravité maladie (Dialyse), inexpérience → avant 2014, < 15 patients/center, petite âge**

- **PC-VAD : gravité maladie(IH, dysfonction VD sévère), chirurgie valvulaire, groupe O (Difficile à greffer)**

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2019 EACTS Expert Consensus on long-term mechanical circulatory support

Evgenij V. Potapov[a,*,†] (EACTS Chairperson), Christiaan Antonides[b,†], Maria G. Crespo-Leiro[c], Alain Combes[d,e], Gloria Färber[f], Margaret M. Hannan[g], Marian Kukucka[h], Nicolaas de Jonge[i], Antonio Loforte[j], Lars H. Lund[k], Paul Mohacsi[l], Michiel Morshuis[m], Ivan Netuka[n], Mustafa Özbaran[o], Federico Pappalardo[p], Anna Mara Scandroglio[q], Martin Schweiger[r], Steven Tsui[s], Daniel Zimpfer[t] and Finn Gustafsson[u,*] (EACTS Chairperson), The Task Force on Long-Term Mechanical Circulatory Support of the EACTS

European Journal of Cardio-Thoracic Surgery 56 (2019) 230–270

- PATIENT EVALUATION AND TIMING OF IMPLANTATION
- PREOPERATIVE ORGAN FUNCTION OPTIMIZATION
- CONCOMITANT CARDIAC CONDITIONS INCLUDING ARRHYTHMIAS
- MANAGEMENT OF NON-CARDIAC COMORBIDITIES
- SYSTEM SELECTION
- ANAESTHETIC MANAGEMENT
- OPERATIVE TECHNIQUE
- PAEDIATRIC OPERATIVE TECHNIQUES
- POSTOPERATIVE MANAGEMENT IN ICU INTENSIVE CARE UNIT
- ANTICOAGULATION
- REHABILITATION
- OUTPATIENT CARE
- MYOCARDIAL RECOVERY
- PUMP THROMBOSIS AND OTHER LATE ADVERSE EVENTS
- AORTIC INSUFFICIENCY AND LATE RIGHT HEART FAILURE
- INFECTION
- END-OF-LIFE CARE

PAEDIATRIC OPERATIVE TECHNIQUES

- **Introduction:** PEDIMACS EUROMACS CF-VAD discharge home
- **Small children – system selection:** CHD, Berlin Heart EXCOR ; CF-VAD > 1.2 m² ; CF vs P VAD → stroke, device failure
- **Single ventricle – Fontan haemodynamics:** case reports, small case series, high mortality ; VAD in Glenn challenge ++ ; FONTAN circulation failure 1) Systemic ventricular failure 2) Failure at level of the CPC ; BiVAD in Fontan after revision of the Fontan pathway
- **TAH:** Transplant or DT ; 70-cc TAH adulte (Approved) – 50-cc TAH complex pediatric cases ; high mortality
- **Special cases:** VAD in CHD with SV ; surgically Corrected TGA (Senning, Mustard) or Corrected Congenital TGA → possible, challenge +++, dedicated heart team discussion ; adult CHD and NON adult CHD = survival

Potapov 2019 EACTS

The European Registry for Patients with Mechanical Circulatory Support (EUROMACS): first EUROMACS Paediatric (Paedi-EUROMACS) report

Theo M.M.H. de By[a,*,†], Martin Schweiger[b,†], Hina Waheed[c], Felix Berger[d], Michael Hübler[b], Mustafa Özbaran[e], Bohdan Maruszewski[f], Carlo Pace Napoleone[g], Antonio Loforte[h], Bart Meyns[i] and Oliver Miera[d], on behalf of the clinicians who contributed data

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Table 1: Present CE-marked mechanical circulatory support systems registered in the EUROMACS database

MCS type	
Durable devices	
Continuous flow	Berlin Heart INCOR
	CircuLite SYNERGY[a]
	HeartAssist 5
	HeartWare HVAD
	Jarvik 2000
	MicroMed DeBakey
	Thoratec HeartMate II
	Thoratec HeartMate 3
Pulsatile extracorporeal	Berlin Heart EXCOR
	Thoratec PVAD
Total artificial heart	SynCardia Cardiowest
Short-term devices	Abiomed AB5000
	Medos DeltaStream[b]
	Levitronix CentriMag[b]
	Maquet CARDIOHELP[b]

Table 3: Patient characteristics preimplant

Characteristics	Total (n = 210)
Age (years), mean ± SD (median, range)	9.3 ± 7.0 (10.5, 0–19)
Preoperative creatinine level (mg/dl), mean ± SD (median, range)	0.83 ± 0.51 (0.70, 0.19 – 3.74)
Preoperative total bilirubin level (mg/dl), mean ± SD (median, range)	0.1 ± 0.1 (0.06, 0.001–0.9)
Body mass index (kg/m^2), mean ± SD (median, range)	17.87 ± 5.08 (16.4, 9.78–37.65)
Age categories, n (%)	
<1 year	38 (18.1)
1–5 years	45 (21.4)
6–10 years	22 (10.5)
>10 years	105 (50.0)
Total	210
Gender, n (%)	
Male	129 (61.4)
Female	81 (38.6)

- **EUROMACS : EACTS ; only Euro-based durable MCS registry for all devices CE Marking in Adults and Children**
- **Transplantation, weaning and death**
- **Retrosepective, 25 H 14 countries </= 19y ; 01/2000 (07/2011) → 12/2017; 237 VADs 210 pts; follow-up 2 years (6 mois-12- mois- 24 mois)**
- **129M (61.4%) 89F (38.6%) 9.3Y 20% < 1Y Dx CMP (CM 55.7% With myocarditis 15.7) 150 (71.4%) CHD 39 (18.6%) other 21 (10.4%); INTERMACS 1-2-3 (21% class 19; inotropes 70.5% 46.8% BH EXCOR 27% HeartWare HVAD Heart Mate II 5.9% HeartAssist5 0.8%**

Table 4: Primary diagnosis

Diagnosis	n	%
Cardiomyopathy	117	55.7
Myocarditis	33	15.7
Congenital heart disease	39	18.6
Coronary artery disease	1	0.5
Valvular heart disease	3	1.4
Cancer	1	0.5
Unknown/missing	16	7.6
	210	

Table 5: Primary and subsequently implanted devices

Devices	1st	2nd	3rd	4th	Total
BiVAD	36	2			38
LVAD	163	12	1		176
LVAD and RVAD	8	1			9
RVAD	1	6	2	2	11
Total artificial heart	1	1			2
Unknown	1				1
Total	210	22	3	2	237

Table 7: Type of ventricular assist devices per age group

	<1	1–5	6–10	>10	Total
LVAD alone					
Pulsatile	32	30	7	14	83
Continuous	2	2	9	68	81
Unspecified		1	1	10	12
LVAD, temporary RVAD					
Continuous LVAD, continuous RVAD				6	6
Pulsatile LVAD, continuous RVAD	2	1			3
BiVAD					
Pulsatile	6	11	5	13	35
Continuous			3		3
RVAD	3	3	3	2	11
Total artificial heart					
Pulsatile		2			2
Unknown				1	1
					237

Table 6: Device strategy at time of implantation, stratified by age categories

	<1 n (%)	1–5 n (%)	6–10 n (%)	>10 n (%)	Total n (%)
Bridge to recovery	4 (8.9)	4 (8.0)	2 (7.1)	7 (6.1)	17 (7.2)
Bridge to transplant	18 (40.0)	23 (46.0)	9 (32.1)	51 (44.7)	101 (42.6)
Destination therapy	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.9)	1 (0.4)
Possible bridge to transplant	14 (31.1)	13 (26.0)	11 (39.3)	36 (31.6)	74 (31.2)
Rescue therapy	3 (6.7)	7 (14.0)	2 (7.1)	7 (6.1)	19 (8.0)
Unknown	6 (13.3)	3 (6.0)	4 (14.3)	12 (10.5)	25 (10.5)
Total	45 (100)	50 (100)	28 (100)	114 (100.0)	237 (100)

- Mean supp time 11.6m
- ICU-LOS 37d 44.3% Home/Rehabilitation facility
- 82.4% Alive at 2Y Transplant 33% 6m 38% 12m

Death 37 pts (17.6%) (1/4 AVC 13.5% MOF) 5.4% Sepsis 5.4% Bleeding 5.4% CP failure, etc

- Survival 12m LVAD 81% BiVAD 63%
- Event free survival 6m 81% 12m 78% 24m 66%
- Survival rate 1Y et 2Y : age 11-19 = 6-11 (86% , > 70%) > 1-5 (69%, 55%) >> < 1Y (54%, 43%)
- Competing outcomes : 24m 51% Transplant

17% Death 9% Wean 22% on VAD

- **Adverse events: using INTERMACS definition**
- **151 AV 38 < 3m 113 > 3m**

- **Device malfunction (pump exchanges for thrombosis) > Infection > Major bleeding (Internal or external bleeding, death, reoperation, hospitalisation, massive transfusion) > neurological events (Stroke; sometimes weaning or transplant after neuro event)**

Table 10: Major adverse event rates

	Within 3 months after implant		More than 3 months after implant	
	Event counts	Events per 100 patient months (CI)	Event counts	Events per 100 patient months (CI)
Device malfunction	20	0.2 (0.1–0.3)	74	4.2 (3.4–5.3)
Major bleeding	6	0.05 (0.02–0.1)	9	0.5 (0.3–1.0)
Major infection	8	0.06 (0.03–0.1)	23	1.3 (0.9–2.0)
Neurological event	4	0.03 (0.01–0.09)	7	0.4 (0.2–0.8)
Total events	38		113	

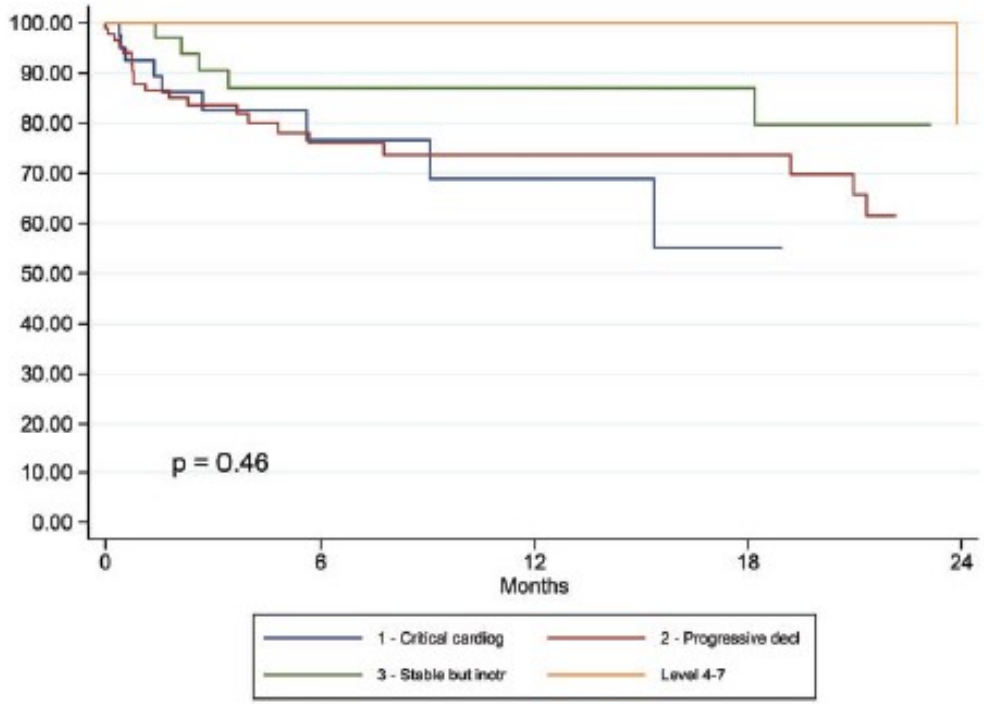

Figure 5: Survival of paediatric patients after primary implantation of a left ventricular assist device or a biventricular assist device, stratified by Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) level.

- EUROMACS registry largest database monitoring children in Europe
- Paedi-EURAMACS ≠ PEDIMCACS (North America) weating time for Heart Transplantation on VAD 33% 6m et 38% 12m Transplanted in Europe vs 50% in PEDIMACS
- Lack of suitable organ donors, small countries, Eurotransplant
- Cumulative competing incidence of death 15% at 1Y 17% at 2Y → Durable VAD FEASIBLE !
- 44% Dicharged
- Bridge to recovery 7.1%, rare; 24/210 pts; bridge to recovery = explanted to recovery → Lack of standardized guidelines ECHO and Hemodynamic for LVAD removal in children
- Neuro events leading cause of death (=PEDIMACS)
- Low stroke early-late in CI-VAD and P-VAD → change in antithrombotic startegy in Edmonton Protocol
- High infection rate (20.5%) More late → prolonged ICU and H LOS
- To be investigated: dicharge, anticoagulation, CHD → 2nd Paedi-EUROMACS

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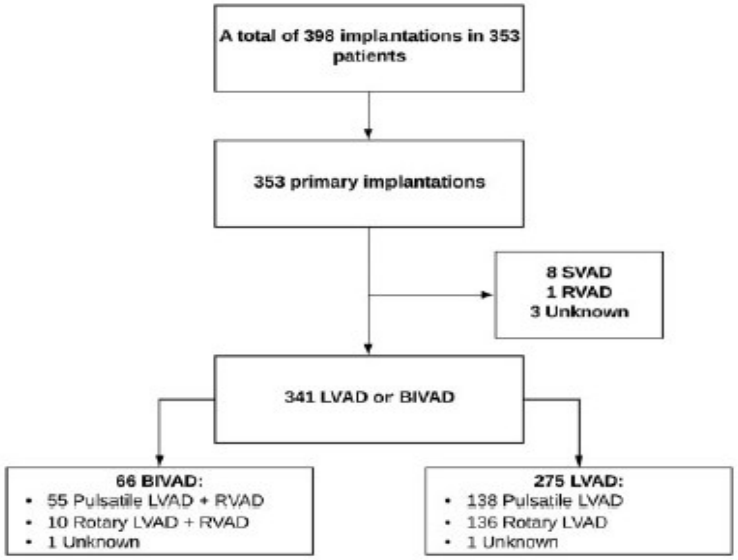
Theo M.M.H. de By[a,*,†], Christiaan F.J. Antonides [b,†], Martin Schweiger [c], Joanna Sliwka [d], Ben Davies [e], Felix Berger [f], Michael Hübler[c], Mustafa Özbaran[g], Bohdan Maruszewski [h], Carlo Pace Napoleone [i], Daniel Zimpfer [j], Eugen Sandica [k], Herwig Antretter[l], Bart Meyns [m] and Oliver Miera [f], on behalf of the clinicians who contributed data

European Journal of Cardio-Thoracic Surgery 0 (2020) 1–13

Table 1: Mechanical circulatory support systems relevant to paediatric populations within EUROMACS

Durable devices	
Continuous flow	HeartAssist 5
	HeartMate II
	HeartWare HVAD
	HeartMate 3
	HeartWare MVAD
	Berlin Heart INCOR
Pulsatile	Thoratec PVAD
	Berlin Heart EXCOR
Total artificial heart	-
Short-term devices	Levitronix CentriMag

EUROMACS: European Registry for Patients with Mechanical Circulatory Support HVAD: HeartWare ventricular assist device; MVAD: miniature ventricular assist device; PVAD: percutaneous ventricular assist device.



1 January 2018, +6/-1 hospitals EUROMACS, 1 July 2019. Total of 29 centres in 15 countries

Now that the follow-up > 8 years, longitudinal outcomes and comparisons between eras <u><2014 and >2015</u> possible

January 2000 - 1 July 2019, 398 implants in 353 patients were registered 150 (42.5%) F and 203 (57.5%) M. Mean age was 8.9Y from 0 to 19 years, with 55 (15.6%) < 1 year

Table 3: Baseline characteristics

	Overall	Era I (n = 156)	Era II (n = 197)	P-value
Age (years)				
Median (range)	10 (0–19)	9 (0.2–19)	10 (0–19)	0.674
Mean ± SD	8.9 ± 6.4	8.8 ± 6.7	9.1 (6.2)	
Sex, n (%)				0.279
Male	203 (57.5)	95 (60.9)	108 (54.8)	
Female	150 (42.5)	61 (39.1)	89 (45.2)	
Age categories (years), n (%)				0.121
1	55 (15.6)	31 (19.9)	24 (12.2)	
1–5	82 (23.2)	34 (21.8)	48 (24.4)	
6–10	53 (15.0)	18 (11.5)	35 (17.8)	
10	163 (46.2)	73 (46.8)	90 (45.7)	
Weight categories (kg), n (%)				0.424
<5	11 (3.2)	5 (3.3)	6 (3.0)	
5–20	139 (40.5)	63 (40.4)	76 (38.6)	
21–40	68 (19.8)	23 (14.7)	45 (22.8)	
41–60	62 (18.1)	31 (19.9)	31 (15.7)	
>60	63 (18.4)	28 (17.9)	35 (17.8)	
Unknown	10 (2.9)	6 (3.8)	4 (2.0)	
Body surface area (m^2)				
Median (range)	1.04 (0.18–2.53)	1.03 (0.21–2.09)	1.04 (0.18–2.53)	0.610
Mean ± SD	1.07 ± 0.58	1.05 ± 0.59	1.08 ± 0.57	
Body mass index (kg/m^2)				
Median (range)	15.8 (8.1–37.7)	15.9 (9.8–31.2)	15.7 (8.1–37.7)	0.489
Mean ± SD	17.0 ± 4.6	17.1 ± 4.4	17.0 ± 4.8	
Total bilirubin levels (mg/dl)				
Median (range)	1.06 (0.03–25.0)	1.00 (0.03–25.0)	1.20 (0.12–25.0)	0.104
Mean ± SD	1.97 ± 3.22	1.76 ± 3.12	2.14 ± 3.31	
Creatinine (mg/dl)				
Median (range)	0.67 (0.20–3.75)	0.67 (0.20–3.75)	0.69 (0.20–2.10)	0.932
Mean ± SD	0.76 ± 0.45	0.79 ± 0.55	0.74 ± 0.36	
eGFR (ml/min/1.73 m^2)				
Median (range)	82 (18–211)	83 (19–153)	82 (18–229)	0.218
Mean ± SD	86 ± 35	80 ± 30	88 ± 38	
Primary diagnosis, n (%)				0.097
Dilated cardiomyopathy	192 (54.4)	81 (51.9)	111 (56.3)	
Congenital heart disease	58 (16.4)	32 (20.5)	26 (13.2)	
Myocarditis	57 (16.1)	28 (17.9)	29 (14.7)	
Restrictive cardiomyopathy	19 (5.4)	10 (6.4)	9 (4.6)	
Hypertrophic cardiomyopathy	4 (1.2)	1 (0.6)	3 (1.5)	
Valvular heart disease	5 (1.4)	0 (0)	5 (2.5)	
Coronary artery disease	1 (0.3)	0 (0)	1 (0.5)	
Cancer	2 (0.6)	0 (0)	2 (1.0)	
Unknown	15 (4.2)	4 (2.6)	11 (5.6)	
INTERMACS patient profile, n (%)				0.671
INTERMACS 1	74 (21.0)	35 (22.4)	39 (19.8)	
INTERMACS 2	175 (49.6)	76 (48.7)	99 (50.3)	
INTERMACS 3	68 (19.3)	35 (22.4)	33 (16.8)	
INTERMACS 4	15 (4.2)	7 (4.5)	8 (4.1)	
INTERMACS 5–7	10 (2.8)	3 (1.9)	7 (3.6)	
Unknown	11 (3.1)	0 (0)	11 (5.6)	
Number of inotropes, n (%)				0.451
0	38 (10.8)	20 (12.8)	18 (9.1)	
1–2	180 (51.0)	76 (48.7)	104 (52.8)	
3–4	66 (18.7)	33 (21.1)	33 (16.8)	
≥5	3 (0.8)	2 (1.3)	1 (0.5)	
Unknown	66 (18.7)	25 (16.0)	41 (20.8)	
Mechanical ventilation, n (%)	87 (25.3)	33 (21.2)	54 (28.9)	0.033
Renal replacement therapy, n (%)	13 (3.8)	8 (5.1)	5 (2.7)	0.301
Circulatory support, n (%)				
IABP	6 (1.7)	3 (1.9)	3 (1.6)	1.000
ECLS	59 (17.2)	22 (14.1)	37 (19.8)	0.077
Device type, n (%)				<0.005
LVAD	275 (77.9)	115 (73.7)	160 (81.2)	
LVAD + temporary RVAD	12 (3.4)	2 (1.3)	10 (5.1)	
RVAD	1 (0.3)	1 (0.6)	0 (0)	
BiVAD	54 (15.3)	37 (23.7)	17 (8.6)	
SVAD	8 (2.3)	1 (0.6)	7 (3.6)	
Unknown	3 (0.8)	0 (0)	3 (1.5)	
Current device strategy, n (%)				0.476
Bridge to transplant	190 (53.8)	80 (51.3)	110 (55.8)	
Possible bridge to transplant	104 (29.5)	46 (29.5)	58 (29.4)	
Rescue therapy	28 (7.9)	15 (9.6)	13 (6.6)	
Bridge to recovery	27 (7.6)	15 (9.5)	12 (6.1)	
Unknown/other	4 (1.1)	0 (0)	4 (2.0)	

- **Primary diagnoses CMP 215 (61%), Myocarditis 57 (16.1%), CHD 58 (16.4%) other 23 (6.5%)**
- **INTERMACS patient profiles 1, 2 and 3 (21%, 49.6% and 19.3%, respectively)**
- **81.3% on inotropic support**
- **25.3% on MV prior to VAD implantation**
- **ECLS 17.2% (IABP 1.7%) prior to VAD implantation**

2-year survival rate
Era 1 71.2% Era 2 65.4%

Table 4: Primary and subsequently implanted devices

Device	First	Second	Third	Fourth	Total
BiVAD	54	2	0	0	56
LVAD	275	20	2	0	297
LVAD, RVAD	12	1	0	0	13
RVAD	1	6	2	1	10
SVAD	8	1	0	0	9
Unknown	3	9	1	0	13
Total	353	39	5	1	398

BiVAD: biventricular assist device; LVAD: left ventricular assist device; RVAD: right ventricular assist device; SVAD: systemic ventricular assist device.

Table 5: Type of primary implanted ventricular assist device per age group

Device set-up	<1	1–5	6–10	>10	Total
LVAD alone					
Pulsatile	41	49	25	23	138
Continuous		6	18	112	136
Unspecified		1			1
LVAD, temporary RVAD					
Continuous LVAD, continuous RVAD				7	7
Pulsatile LVAD, continuous RVAD	2	2	1		5
BiVAD					
Pulsatile	8	16	6	20	50
Continuous		1	2		3
Unspecified		1			1
SVAD					
Pulsatile				2	2
Continuous		2		3	5
Unspecified				1	1
RVAD					
Unknown				1	1
Unknown		1	1	1	3

BiVAD: biventricular assist device; LVAD: left ventricular assist device; RVAD: right ventricular assist device; SVAD: systemic ventricular assist

Table 6: Congenital heart diseases (70 diagnoses in 59 patients)

Congenital heart disease	*n*
Complete atrioventricular septal defect	5
Transposition of the great arteries	8
Hypoplastic left heart	7
Single ventricle	4
VSD/ASD	14
Tetralogy of Fallot	1
ALCAPA	3
Ebstein's anomaly	1
Left heart structural/valvular	3
Other/unknown	24

ALCAPA: anomalous left coronary artery from the pulmonary artery; ASD: atrial septal defect; VSD: ventricular septal defect.

70 patients: 1/multiple concomitant cardiac procedure(s) (12 CHD, 19 valve procedures, 47 other procedures)

•51.6% Berlin Heart EXCOR, 31.7% HeartWare HVAD 4.8% HeartMate II 3.7% HeartMate , 0.6% HeartAssist5

Table 7: Device strategy at the time of first implant, stratified by age categories

Device strategy	<1	1-5	6-10	>10	Total
Bridge to recovery	8	7	2	10	27
Bridge to transplant (patient currently listed for transplant)	28	47	25	90	190
Possible bridge to transplant	16	20	21	47	104
Rescue therapy	2	7	4	15	28
Unknown/other	1	1	1	1	4
Total	55	82	53	163	353

Table 8: Primary causes of death

Primary cause of death	n (%)
Neurological dysfunction	26 (38.2)
Multiorgan failure	13 (19.1)
Major bleeding	4 (5.9)
Major infection	4 (5.9)
Cardiopulmonary failure	3 (4.4)
Device malfunction	2 (2.9)
Right heart failure	1 (1.5)
Other	7 (10.3)
Unknown/missing	8 (11.8)
Total	68

83.3% VAD intention to transplant (bridge to transplant or possible bridge to transplant)

- **Median support time 4.2 months (0–83.6 months). Median ICU LOS 22 days (0–422 days) 265 (80%) children survived 2-year follow-up**
- **6m 33.2% 12m 46.7% 57.5% 2Y transplanted post VAD implantation**
- **68 patients died (38.2% died of cerebrovascular accidents, 19.1% MOF)**

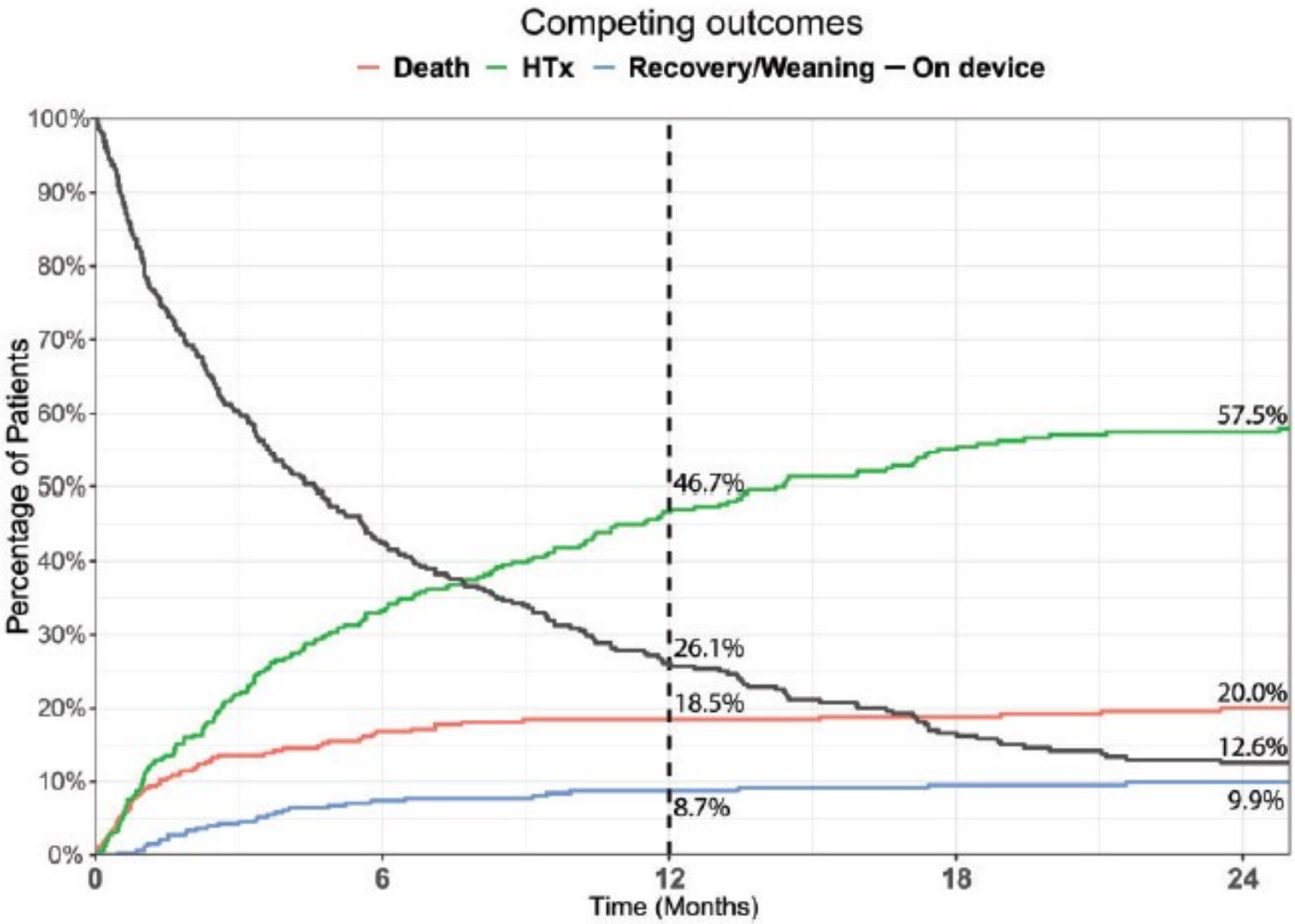


Figure 2: Competing outcomes analysis for death, heart transplant, recovery/weaning or patients on device support. HTx: heart transplant.

2nd Paedi-EUROMACS

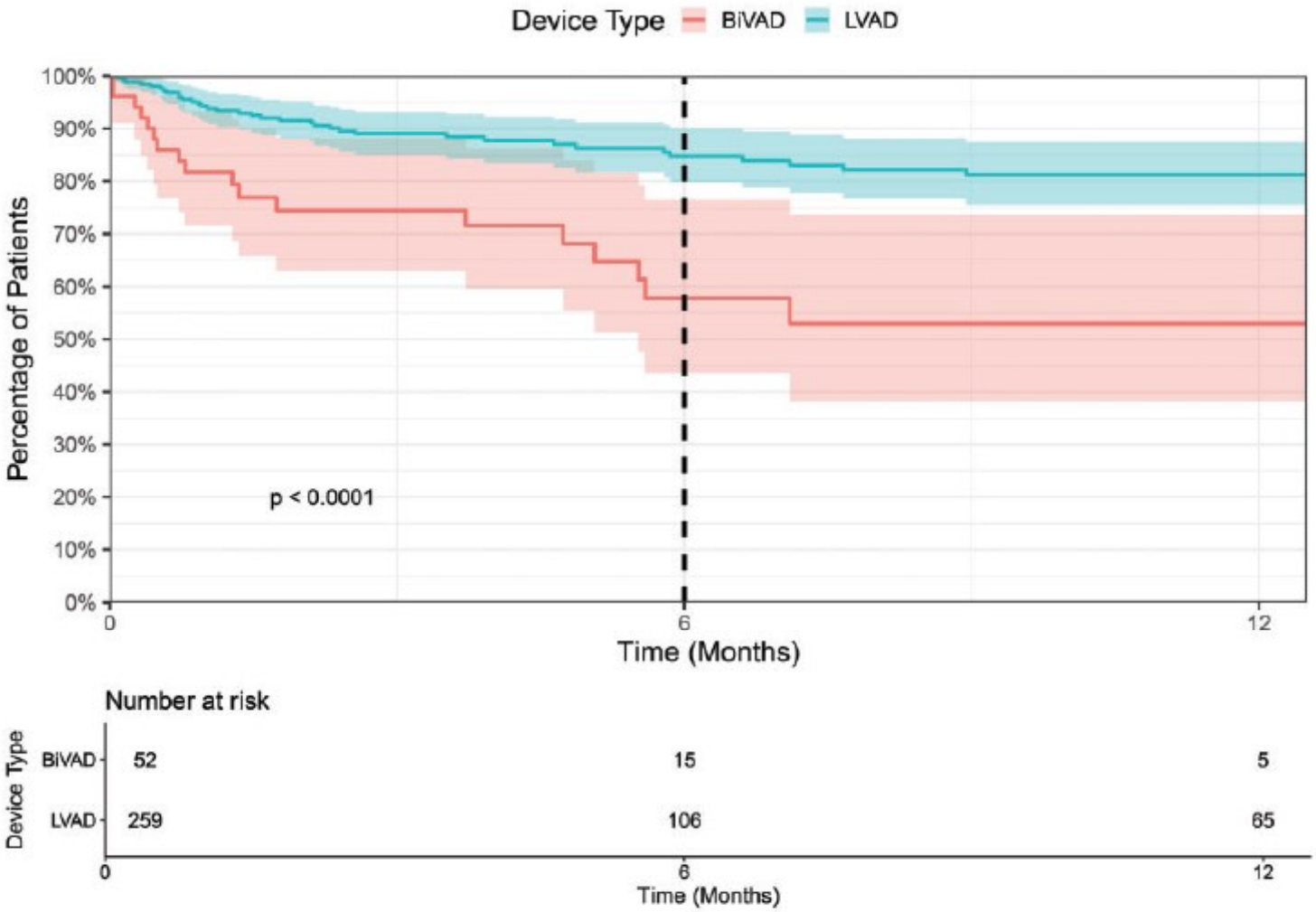


Figure 3: Survival analysis of LVAD versus BiVAD. BiVAD: biventricular assist device; LVAD: left ventricular assist device.

- **Survival all patients with MCS 79.9% 6m 75.5% 12m 67.9% 2 years**
- **Stratified for device type Survival 1 year 81.3% for LVADs 52.9% for BiVADs**

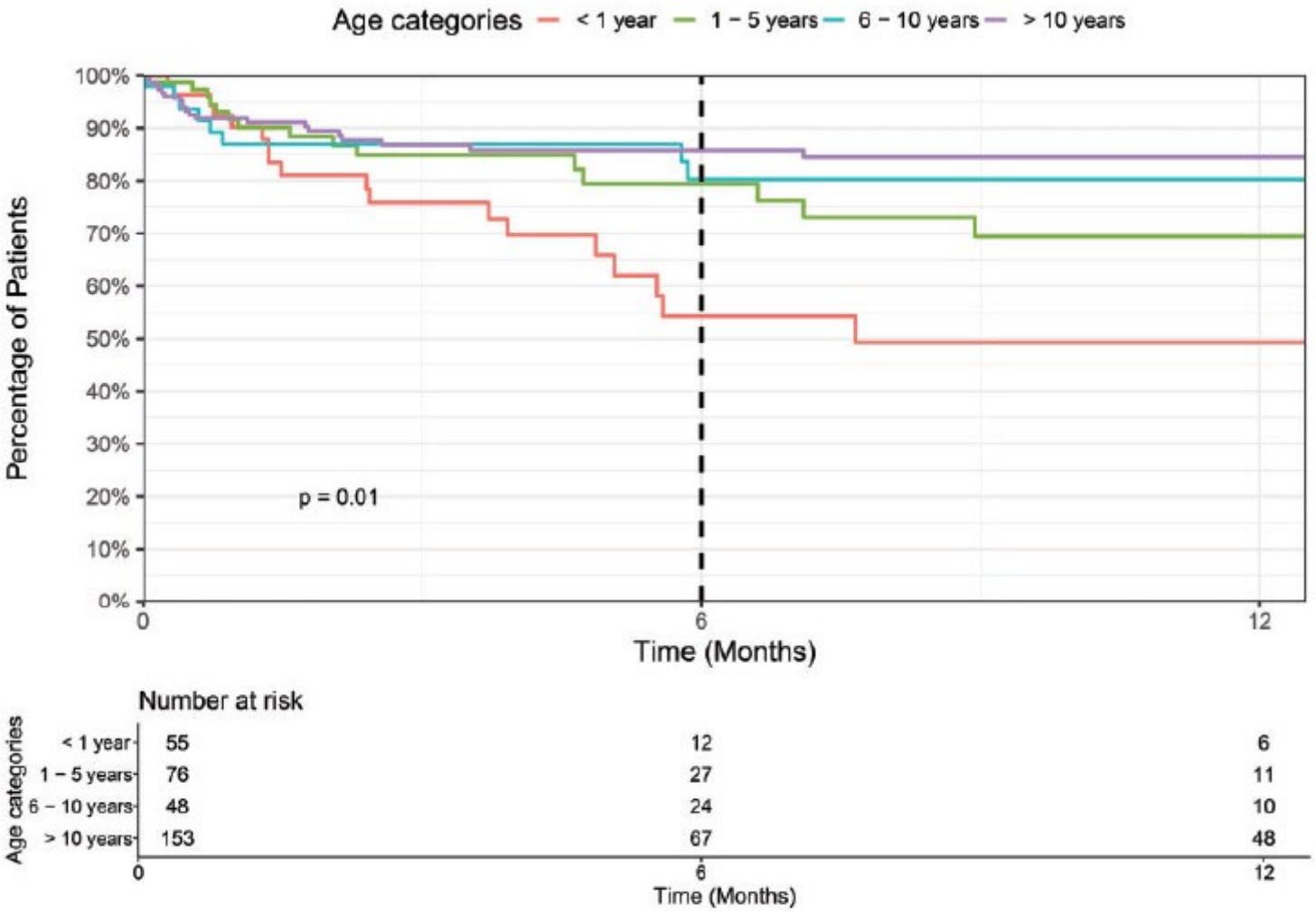


Figure 4: Survival analysis by age category.

Stratified by age, 11–19Y survival rate 1Y 84.5% 2Y 78.4% 6–10Y survival rate 1Y 80.3% 1–5Y survival rate 1Y 69.4% <1 year old poorest survival rate of 49.3% at 1 year (P = 0.01)

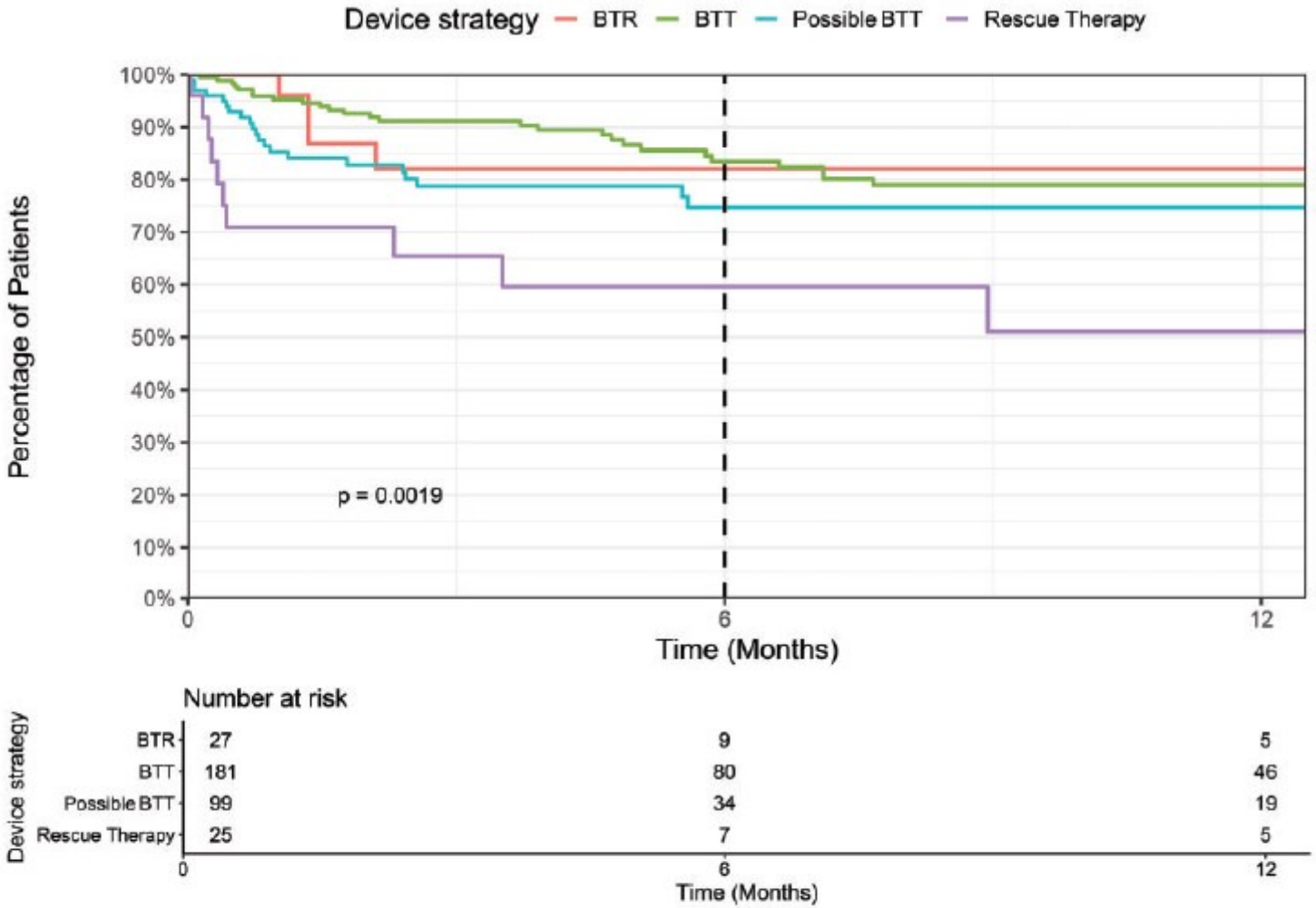


Figure 5: Survival analysis by device strategy. BTR: bridge to recovery; BTT: bridge to transplant.

1-year survival rate stratified by device strategy survival rates 82% bridge to recovery, 78.9% for bridge to transplant, 74.7% for possible bridge to transplant worst survival rate (51%) for rescue therapy (P = 0.0019)

2nd Paedi-EUROMACS

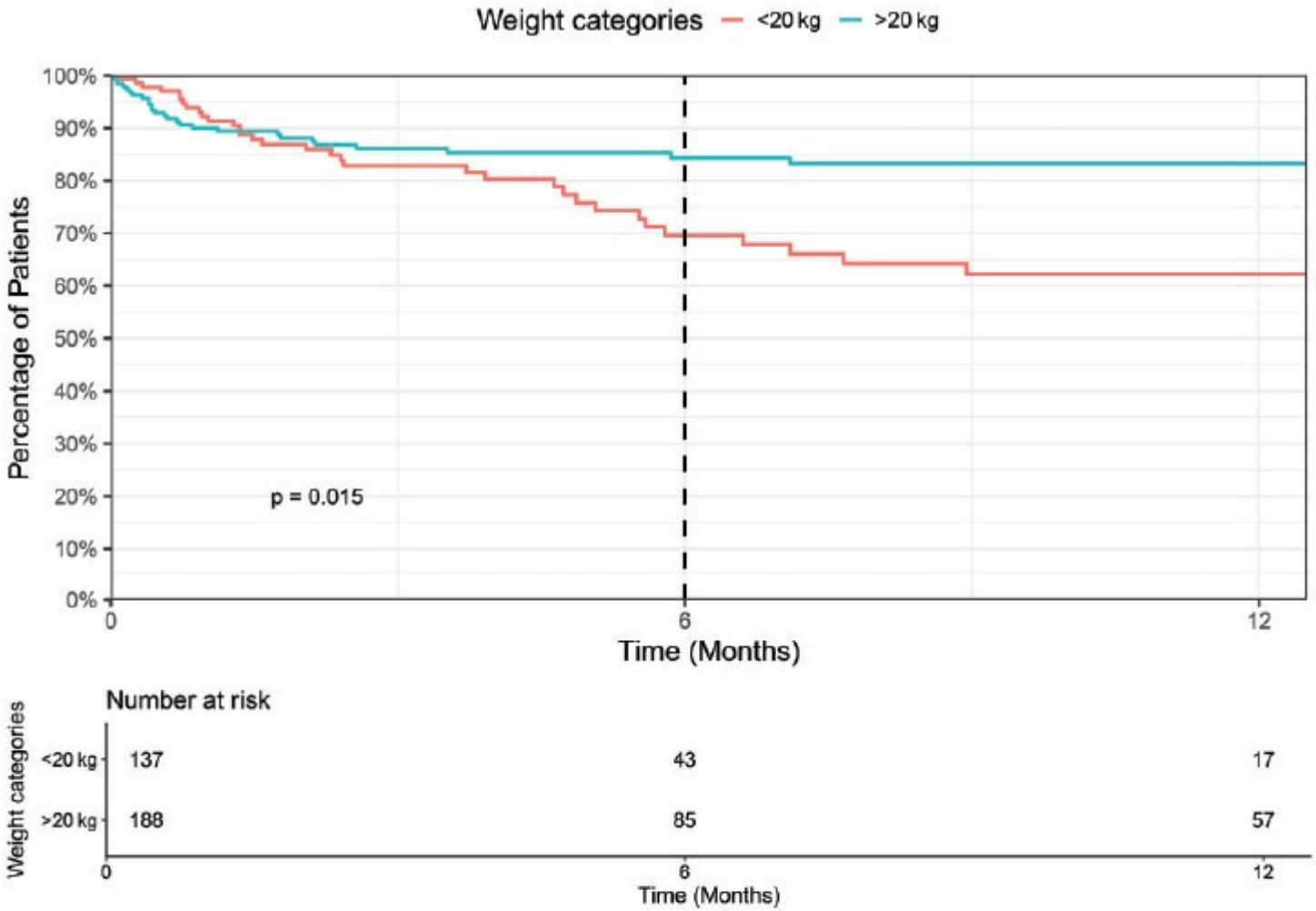


Figure 6: Survival by weight: below 20 kg or 20 kg and above.

Significantly worse survival rate for patients weighing <20 kg (P = 0.015)

2nd Paedi-EUROMACS

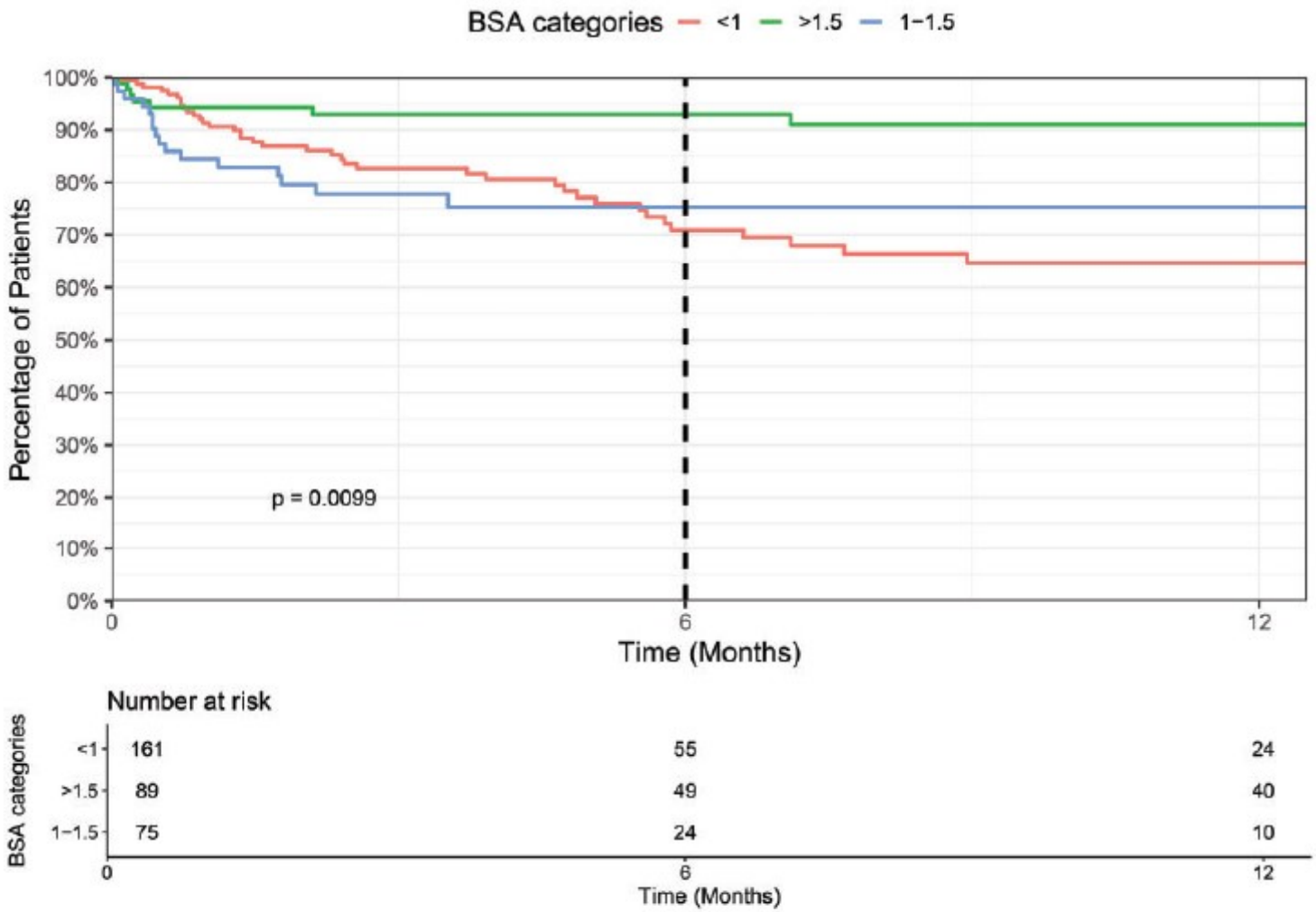
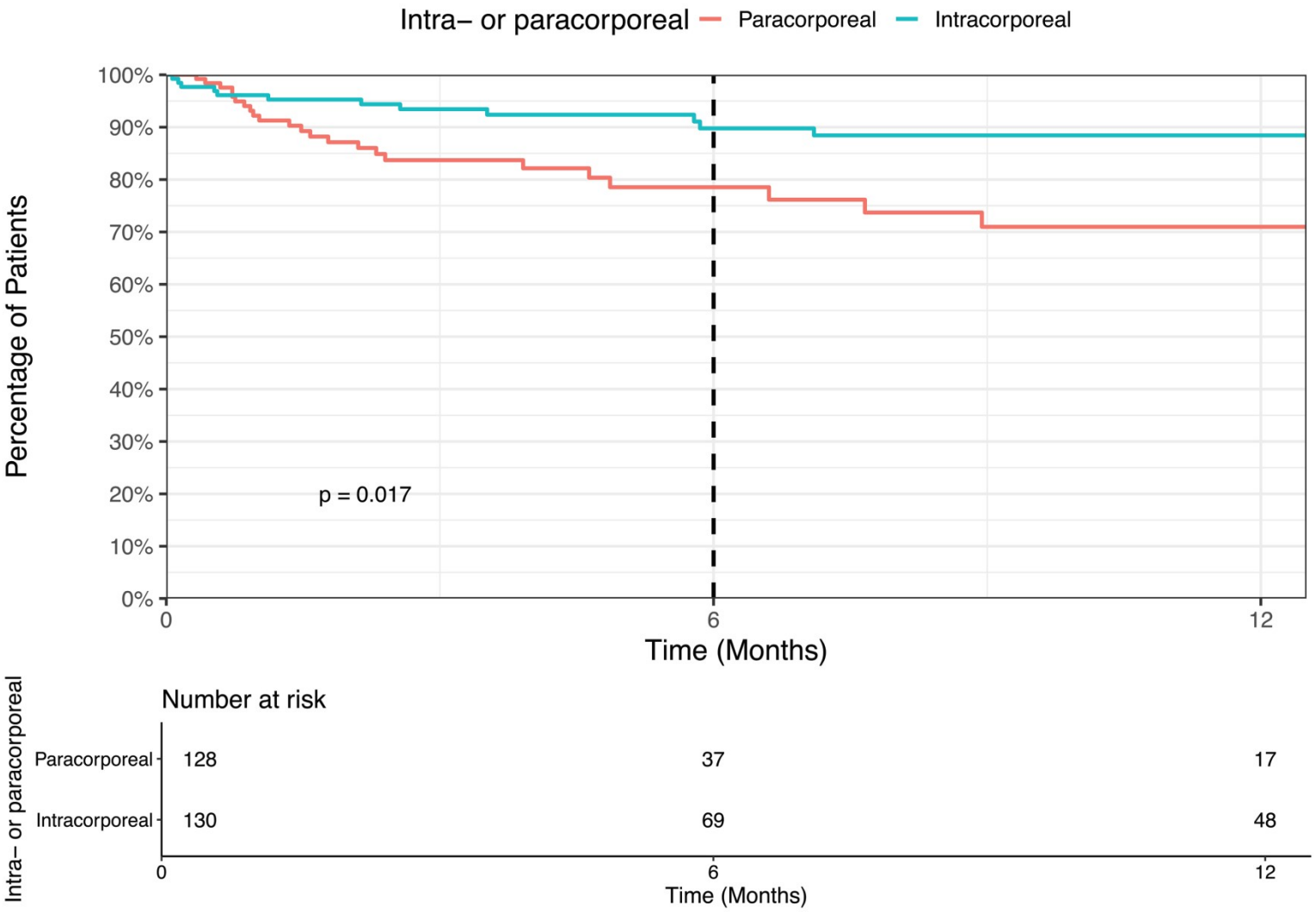


Figure 7: Survival stratified by BSA. BSA: body surface area.

Patients lower BSA (<1m2 or between 1 and 1.5m2) worse survival rate than patients with a BSA >/= 1.5m2 (P = 0.0099)

2nd Paedi-EUROMACS



Supplementary Figure 3: Survival by intra- or paracorporeal device type.

P-VAD compared to CF-VAD device significantly worse survival for paracorporeal support (71% vs 88%; P = 0.017)

2nd Paedi-EUROMACS

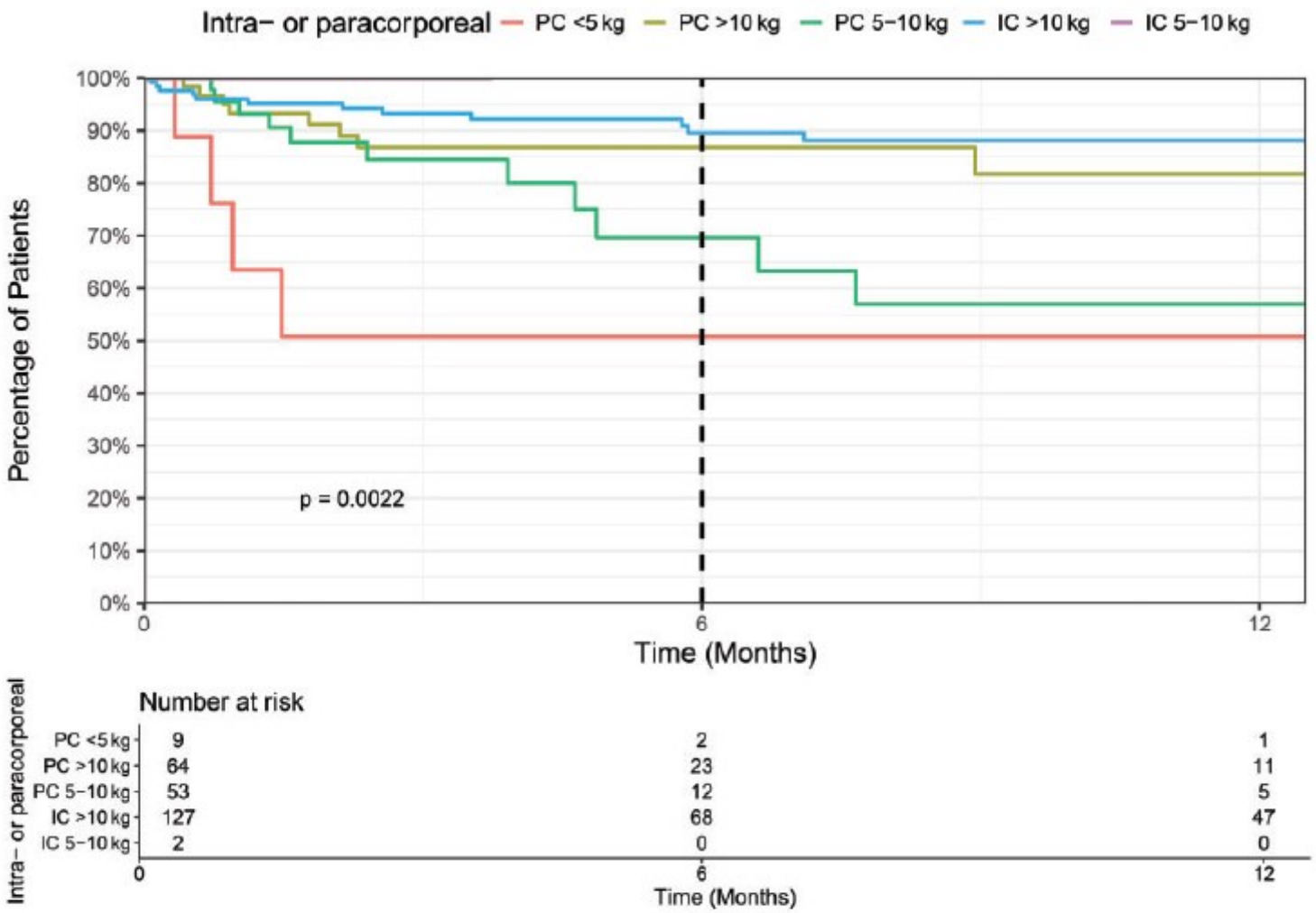


Figure 8: Survival for IC versus PC devices by weight category. IC: intracorporeal; PC: paracorporeal.

Groups intracorporeal and paracorporeal devices separated by weight categories, >10 kg do not have a significantly different outcome but do differ significantly between weight categories (P = 0.0022)

2nd Paedi-EUROMACS

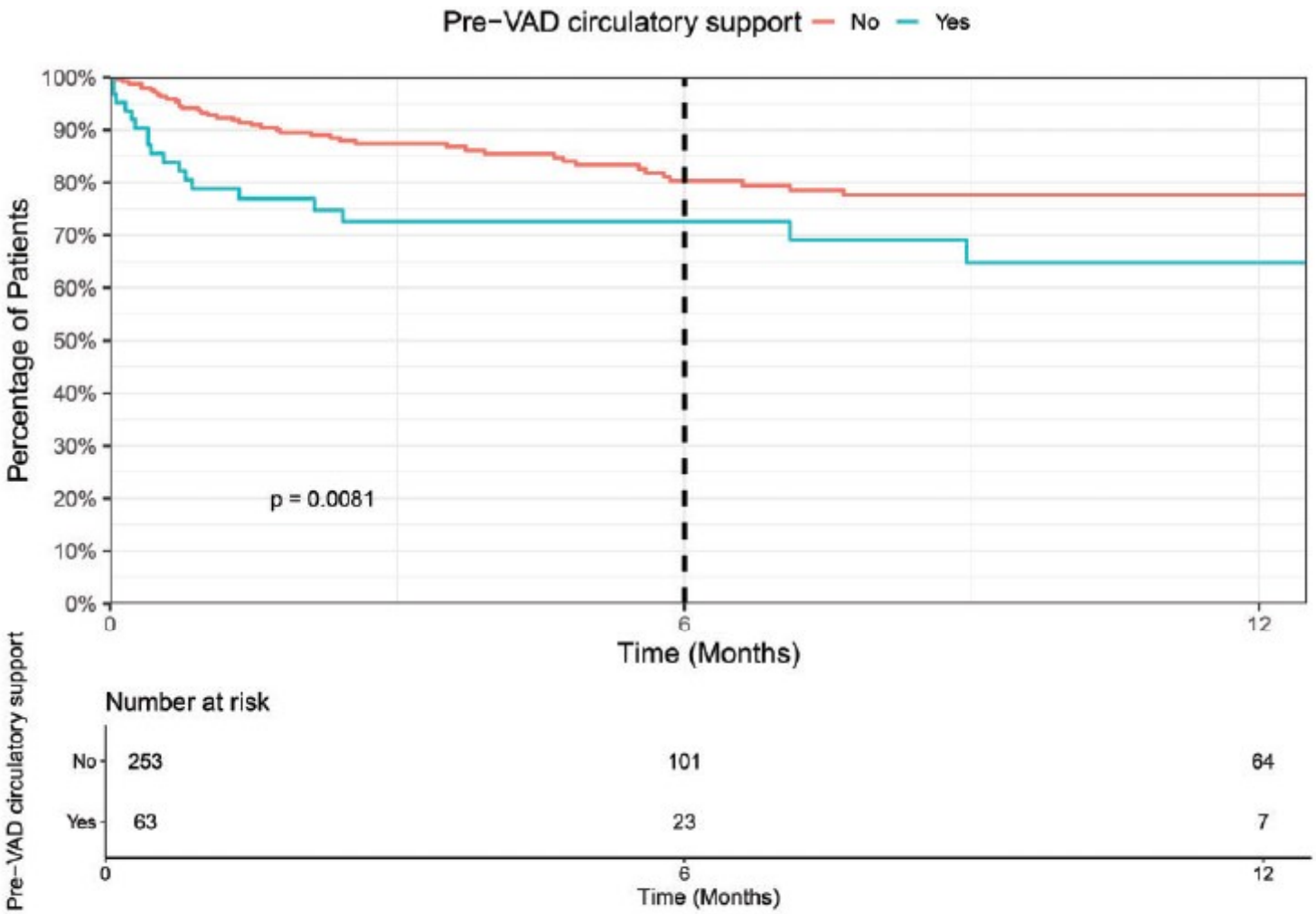


Figure 9: Survival of patients stratified by pre-VAD implant circulatory support. VAD: ventricular assist device.

A comparison of survival rates of patients with or without ECLS/IABP with support have a significantly worse outcome (P = 0.0081)

Table 9: Univariable and multivariable analyses of baseline predictors for death

Characteristics	Univariable		Multivariable	
	Hazard ratio (95% CI)	*P*-value	Hazard ratio (95% CI)	*P*-value
Age (years)				
<1	Reference		Reference	
1–5	0.51 (0.25–1.06)	0.07	0.40 (0.19–0.84)	0.02
6–10	0.39 (0.17–0.89)	0.03	0.48 (0.21–1.09)	0.08
>10	0.28 (0.14–0.55)	< 0.001	0.32 (0.16–0.64)	0.001
Device strategy				
Bridge to transplant	Reference		Reference	
Bridge to recovery	1.07 (0.38–2.99)	0.89	1.08 (0.38–3.06)	0.88
Rescue therapy	2.82 (1.38–5.77)	0.004	3.24 (1.56–6.74)	0.002
Device type				
BiVAD	Reference		Reference	
LVAD	0.33 (0.19–0.58)	<0.001	0.37 (0.20–0.68)	0.001

- **Older patients and patients supported by an LVAD (compared to BiVAD) lower risk of death**
- **Patients rescue therapy had a significantly higher risk of death**
- **Compared to patients <1 year old, the HR for death was statistically significant for patients aged 1–5 years: 0.40 and for patients >10 years: 0.32, trended towards significance for patients aged 6–10 years**
- **Rescue remained a predictor for a significantly worse survival rate**
- **T he use of an LVAD was associated with a lower probability of death**

Table 10: Major adverse events

Major adverse events	Within 3 months		After 3 months		Total
	Event counts	Events per patient-year	Event counts	Events per patient-year	
Device malfunction	106	1.69	107	0.60	213
Major bleeding	30	0.48	7	0.04	37
Major infection	40	0.64	62	0.35	102
Neurological dysfunction	49	0.78	24	0.13	73
Total	225		200		425

- **425 adverse events were reported during VAD support**
- **< 3 months 225 events 200 > 3 months**
- **Most frequently device malfunction 106 times < 3 months which resulted in 1.69 events per patient-year**
- **After 3 months, 0.60 device malfunctions per patient-year were reported**
- **Event rates for neurological dysfunction and infection were 0.78 (n = 49) and 0.64 (n = 40) per patient-year, respectively, for the first 3 months.**
- **After 3 months, 0.13 events of neurological dysfunction (n = 24) and 0.35 infections per patient-year (n = 62)**
- **30 events of major bleeding < 3 months (0.48 events per patient-year) and 7 events after 3 months (0.04 events per patient-year)**

- 2nd more details than 1th Paedi-EUROMACS, demographic characteristics =
- Differences PEDIMACS --- 2nd Paedi-EUROMACS: INTERMACS 1 33% vs 21%;
- MV 45% vs 25.3%; ECLS 12.6% vs 17.2%
- PEDIMACS early transplant vs 2nd Paedi-EUROMACS at 6 months (50% vs 35%) at 12m 51.4% vs 46.7%
- 2nd Paedi-EUROMACS > Adverse Events than 1th Paedi-EUROMACS (Sicker ??)
- BiVAD Era 1 23.7% vs Era 2 8.6%
- Class at high risk < 1y in al reports (Europe = North America)
- < 20 kg high risk
- > 10 kg P-VAD = CF-VAD about mortality
- < 1 m2 of BSA → mismatch ventricle of BH EXCOR with BSA → > thromboembolic events
- Better mortality in CHD
- Higher mortality in myocarditis
- PEDIMACS registry in North America MANDATORY not in Europe for EUROMACS

Anticoagulation

- Changement du fétus à l' âge adulte : le concept de *developmental hemostasis*
- Principales changements premières 6-12 mois, encore jusqu'à 16 ans
- Naissance : [protéines coagulations] 50% des adultes
- Facteurs ↑ progressivement
- FVII encore plus de temps
- [Fibrinogène] : naissance VN → ↓ 6—12 mois → 1-5 ans VN
- ATIII signif ↓ naissance → 3-6 mois, normalisation > 1 ans
- Protéine C ↓ naissance, VN à 16 ans
- Protéine S ↓ naissance, VN après 3 mois
- Plasminogene ↓ naissance, VN > 6 mois
- t-PA et D-dimeres ↑

Table 4. Coagulation parameters in neonatal and childhood *vs.* adult. Summary of test results and potential effect on hemostasis. For details, see Developmental hemostasis part

Component	Parameter	Neonatal period (mean value)*	Normalization	Net effect on hemostasis
Primary hemostasis	Platelets	Normal or increased	1 year (after transient increases)	Enhanced primary hemostasis
	von Willebrand factor	Increased (153%)*	3 months	
	Platelet closure time (PFA-100®)	Shortened	2–4 weeks	
Coagulation	FII, FVII, FIX, FX	Decreased (40–66%)*	1 year (up to 16 year for FVII)	Decreased coagulation potential
	FXI, FXII, PK, HMWK	Decreased (37–54%)*	1 year	
	FV	Normal or decreased (70%)*	1 year (up to 16 year)	
	FVIII	Normal or increased (100%)*	1 month	
	Fibrinogen	Decreased ** or normal	1 year	
	PT	Prolonged or normal	1 year	
	aPTT	Prolonged	1 year (up to 16 year)	
Natural coagulation inhibitors	Antithrombin	Decreased (63%)	3 months	Decreased regulatory/ inhibitory potential
	Protein C	Decreased (35%)	16 years	
	Protein S	Decreased (36%)*	3 months	
Fibrinolysis	Plasminogen	Decreased (36%)*	6 months	Increased fibrinolytic activity
	Alpha 2 antiplasmin	Normal or decreased (85%)*	6 months	
	tPA	Increased	1 week	
	D-dimer	Increased	16 years	

Toulon, Int. Jnl. Lab. Hem. 2016, 38 (Suppl. 1), 66–77

Problemes vs solutions

- Interaction surface sang ↔ éléments externes du circuit → Compatibilité des circuits
- Activation de la chaine de la Coagulation → Médocs AntiCoagulants (Efficacités, dosage ↔ surdosage, effets collatéraux)
- Activation des plaquettes → Médocs antiagrégants
- Réponse inflammatoire systémique → stéroïdes ?
- Infection → prévention et traitement
- Acquired vWS dans les patients avec VADs

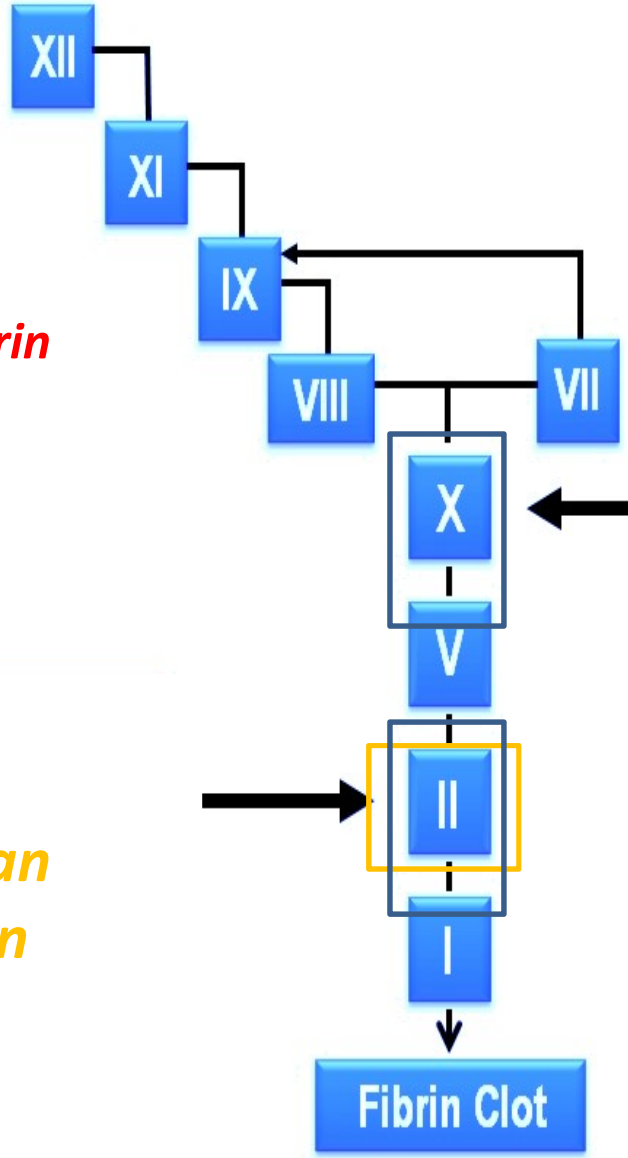
Médicaments AC et interactions

AC
↓
INIB activ C
↓
Eviter EI sur VAD

Unfractionated heparin
Enoxaparin
- FII, FX, FIX, FXI, FXII

Warfarin
- FII, FVII FIX, FX

Argatroban
Bivalirudin
- FII



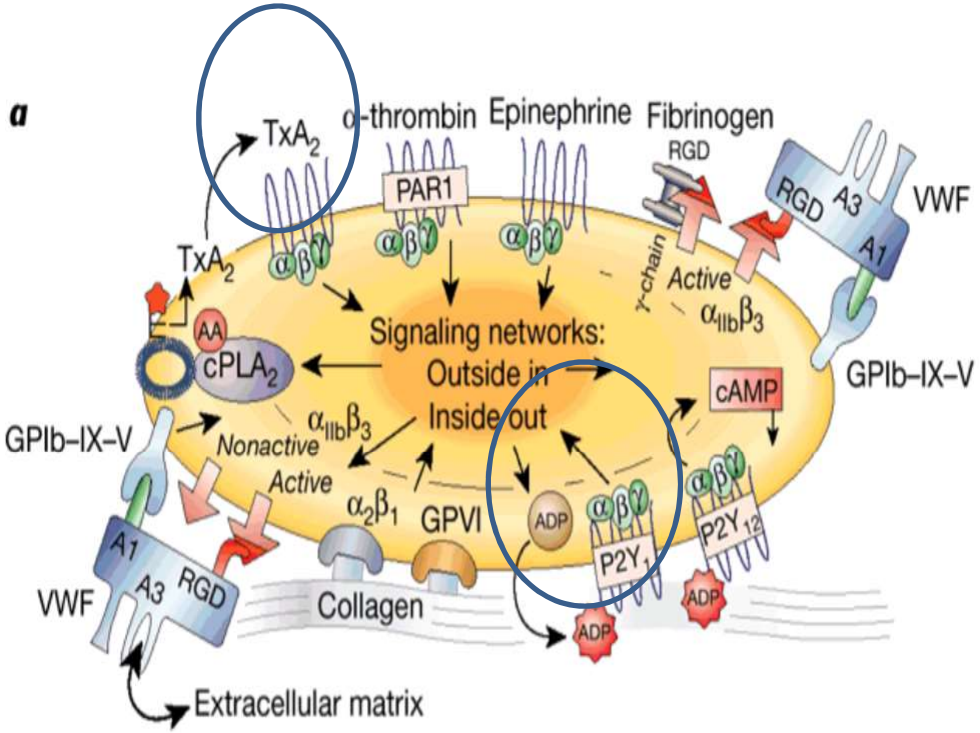
Héparine non fractionée (UFH)
- Besoin rempl ATIII
- Resistance
- Limitations PK pour lien proteins plasma (PF4)
- Risque TIH (NN 0-1.7%, Enfants 1.3-52%)

HBPM
- Ponction BID, long term QOL
- Demi-vie long, no rev agent

Warfarin (→VKOR Enzime)
➢Interactions, alimentation, diff AND, Infections

Bivalirudin, Argatroban
>No reversal agent
>Little data

Limitations antiaggregants : quel agent ? Dosage ?



Arachadonic acid Pathway
ASA

ADP receptors
Clopidogrel
Dipyridamole

PDE
Pentossifilline (TAH)

SANG ↔ Materiel → activation hémostase, plaquettes, etc
+ debit non lineare, stress parois → activation PLT

Axial LVAD x100 plus haut stress de parois que arterioles
Jaffer et al J Thromb Haemost 2015

EI associés à l'hémostase

Hémolyse

- Marqueur traumatisme CG pour « shear stress », débit turbulent ou thrombose du VAD
- Temporary VAD, IC axiale, roller pump (ECMO) > IC et EC-VAD avec pompe centrifuge
- Labo : ↓ Hb (TAH 5-7 g/dl→ transfusion) ↑ Hb plasmatique (> 40 mg/dL) **Ramirez A J Extra Corpor Tachnol 2016**

  ↑ LDH (Signe précoce; si > 1000 UI/ml ou dysfonction pompe → Changer pompe)
- Hb pl↔vWF A2 → thrombose pompe du VAD
- Hb pl → ↑adhésion PLT ↔ vWF A1 ↔ Fibrinogéne → thrombose pompe du VAD

Birschmann I JHLT 2014 Kirklin JK JHLT 2015 Da Q Blood 2015

Thrombose

- Canules EXCOR transparents : facile localisation
- Dimensions, position, couleur, mobilité thrombus
- Changement BH-EXCOR pump bedside, canule OR
- Risque AVC ischémique (Evolution hémorragique) ou TE arteriel NON SNC
- IC → thrombose ↔ hémolyse → dx Clinique+ LABO
- Minor hemolysis LDHx2.5 et Hbpl > 20 mg/dL
- Episode HEMOLYSE : Hb pl > 40 symptoms HF ↓Hb et dysfonction pompe

Gravlee CPB and MCS: Principles and Practice 2016 Fraser NEJM 2012

Thrombose

- Fonction pompe : VAD speed- Power spikes
- Jarvick 2015 : dx thrombose = Hb pl + Clinique
- HeartWare : changements pump power-rotor speed-estimated flow → évaluation/diagnostic
- Treatement thrombose : héparine IV (Résolution 23%), Bivaluridine/Argatroban (56%) Thrombolyse (Haut risque hémorragique)
- IC dysfonction (princ thrombose) 16% (x2 que adultes)
- Facteurs ↑ risque thrombose : différences anatomiques (Ventricules petits, VD en position systémique, dextrocardie), causes différentes de HF, différences hémostase P-A

Jorde UP JACC Heart Failure 2015 Dang G ASAJO 2017 Roenthal DN JHLT 2016

Thrombose

Facteurs ↑ risque thrombose : différences anatomiques (Ventricules petits, VD en position systémique, dextrocardie), causes ≠ insuffisance cardiaque hémostase Péd ≠ Ad

1) Facteurs liés aux patients :

-- âge, BMI, SC, sexe

-- cardiopathie congénitale type cyanogène

-- thrombophilie congénitale ou acquise

2) Facteurs liés au management du patient

-- Traitement antiaggrégant (Efficacité)

-- positionnement pompe et position des canules (Zones de stasis → > risque de formation thrombus)

-- Pompe travail à vitesses basses

-- HTA non contrôlée

3) Facteurs associés au design de la machine/pompe

ASAIO Journal 2019

Bivalirudin Experience in a Heterogeneous Ventricular Assist Device Population

Angela Bates,* Holger Buchholz,† Darren Freed,† Roderick MacArthur,† Tara Pidborochynski,‡ and Jennifer Conway‡

- **Successful use BIVALIRUDINE in Prevention and Management of pump THROMBOSIS with 10 HeartWare, 5 HeartMate II, 2 BH Excor**
- **14 pts, 17 episodes, 92% M, age 15d-67y median age 45y, 5 pts < 18y**
- **aPTT - dosage Bivalirudine, LDH Dx thrombose et efficacité**
- **Adverse Events (Reactions, beleeding, neuro events)**
- **Efficacy to treat**
- **Rescue therapy**
- **Median start after VAD insertion 116d (3-1870d)**

Table 1. Patient Characteristics of VAD population on Bivalirudin

Episode No.	Age	Type of VAD	Days Before Bivalirudin*	Days of Bivalirudin	Indication for Bivalirudin	Anticoagulation Before Bivalirudin	Complications on Bivalirudin	Outcome†
1	15 days	Berlin EXCOR	3	113	Suspected HIT	Heparin	None	Death
2	1 year	Berlin EXCOR	35	44	Inadequate heparin levels/pump thrombosis	Heparin	None	Transplant
3	5 years	HeartWare LVAD	21	38	Suspected pump thrombosis	Heparin	None	Transplant
4	7 years	HeartWare LVAD	68	3	Confirmed thrombosis	Heparin	Suspected pump thrombosis	Pump replaced
5	7 years	HeartWare LVAD	170	7	Confirmed thrombosis	Warfarin	None	Transplant
6	10 years	HeartWare LVAD	30	43	Confirmed thrombosis	Heparin	DLI; VAP	Discharge on warfarin
7	10 years	HeartWare LVAD	661	40	Suspected pump thrombosis	Warfarin	DLI; VAP suspected pump thrombosis	Pump replaced
8	20 years	HeartMate II LVAD	82	39	Confirmed thrombosis	Heparin	Minor bleed: GI bleed	Discharge on warfarin
9	43 years	HeartMate II LVAD	62	68	Coagulopathy	Heparin	Major bleed: SDH secondary to fall	Discharge on warfarin
10	43 years	HeartWare LVAD	172	20	Acute kidney injury	Heparin	None	Death
11	47 years	HeartWare LVAD	136	3	Suspected pump thrombosis	Heparin	Minor bleed: GI bleed	Death
12	47 years	HeartWare LVAD	6	9	Suspected pump thrombosis	Warfarin	None	Discharge on warfarin
13	51 years	HeartWare LVAD	158	13	Suspected pump thrombosis	Warfarin	None	Discharge on warfarin
14	51 years	HeartWare LVAD	179	7	Suspected pump thrombosis	Warfarin	None	Discharge on warfarin
15	60 years	HeartMate II LVAD; HeartWare RVAD	3	21	Suspected pump thrombosis	Heparin	None	Death
16	60 years M	HeartMate II LVAD	1,870	7	Suspected pump thrombosis	Warfarin	Minor: BRBPR (hemorrhoids)	Discharge on warfarin
17	67 years M	HeartMate II LVAD	149	48	Suspected pump thrombosis	Warfarin	None	Discharge on warfarin

*These periods refer to days of admission to hospital before bivalirudin was initiated as primary anticoagulation strategy.
†Outcome following discontinuation of bivalirudin infusion; some patients remained on bivalirudin until death, which is indicated in the table.
BRBPR, ; DLI, ; GI, ; HIT, ; LVAD, left ventricular assist device; RVAD, right ventricular assist device; SDH, ; VAD, ventricular assist device; VAP, .

Bates ASAIO 2019

Table 2. Indications for the use of Bivalirudin in Long-Term VADs

Indications for Bivalirudin	No. of Patient Episode(s)
Suspected or confirmed pump thrombosis	13
Suspected HIT	1
Coagulopathy on UFH	1
AKI	1
Inadequate heparin levels	1

AKI, ; HIT, ; UFH, unfractionated heparin; VAD, ventricular assist devices.

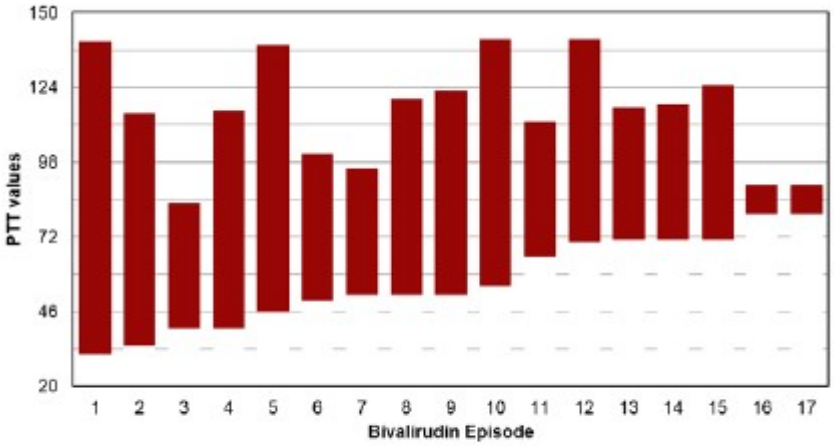


Figure 1. Range of PTT values in patients with long-term VADs during each bivalirudin episode. PTT, partial thromboplastin time; VAD, ventricular assist devices.

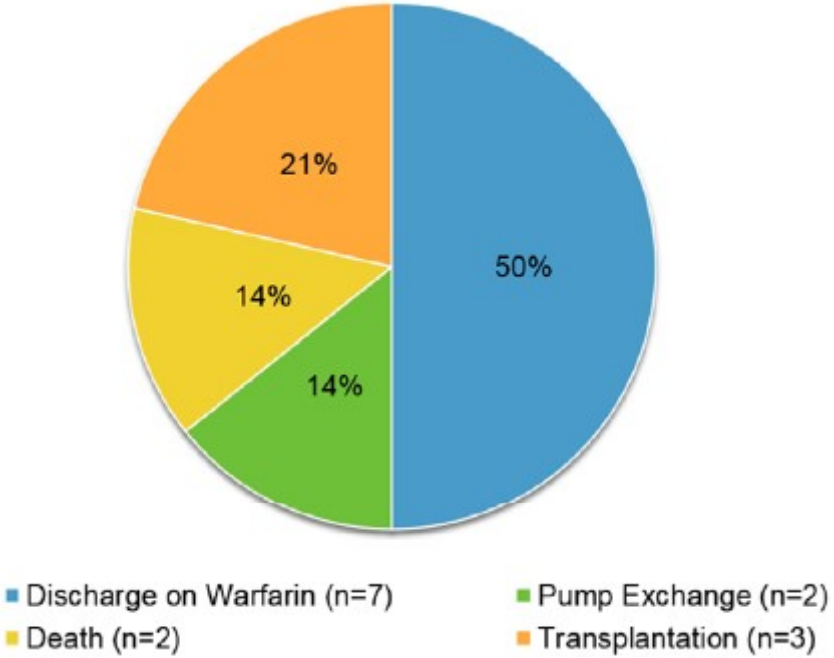


Figure 2. Outcomes following suspected pump thrombosis.

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- Early start (LDHx2.5N) vs Late (LDH > 3.2xN)
- Bivalent DTI 1) Inhibition circulating and fibrin-bound Thrombin wich is reversible) 2) Inhibition Platelet Adhesion
- Less immunogenic tha heparine
- Attention: aPTT verify good performed
- Short half-life (30m)
- Less risk of bleeding
- Indipendent by AT
- Optimal profile in standerd use (Thromobosis in first 3 months +++)
- Disavantages : more fibrin/thormbus in stagnant flow (Off-pump insertion), ECMO pigtails, low-flow state; daily fluctuation
- Early use is better
- Difference pediatric vs adult in pharmacology
- More studies for safety, efficacy

Bates ASAIO 2019

A Review of Bivalirudin for Pediatric and Adult Mechanical Circulatory Support

Tori Taylor[1] · Christopher T. Campbell[2] · Brian Kelly[3]

American Journal of Cardiovascular Drugs 10 November 2020

Table 1 Medication details

	Heparin [31]	Bivalirudin [32]
Mechanism of action	Potentiates the activity of antithrombin III to inactivate thrombin	Reversible direct thrombin inhibitor
Half-life	1.5 h[a]	Normal renal function: 25 min Severe renal impairment: 57 min
Metabolism/elimination	Depolymerization and desulphation via the reticuloendothelial system in the liver and spleen; some renal elimination	Proteolytic cleavage; excreted 20% in urine
Monitoring	aPTT; anti-factor Xa activity; ACT	aPTT; ACT
Complications (noted > 10%)	HIT; heparin resistance	Hypotension, pain, headache, back pain
Reversal [33, 34]	Protamine	Factor VII; hemofiltration
Cost per day ($US) [10]	6	303

Table 3 Review of literature in patients with ventricular assist devices (VAD)

Study	Sample size and population	Study design	Anticoagulant dose and therapeutic targets	Outcomes
Ljajikj et al. [24]	57 adult pts undergoing LVAD implantation on ECLS; 21 pts with HIT received bivalirudin; 36 non-HIT pts received heparin	Retrospective case–control	In pts with ACT <160 s, bivalirudin bolus of 0.5 mg/kg, followed by infusion of 0.5 mg/kg/h. In pts with ACT >160 s, bivalirudin bolus of 0.25 mg/kg, followed by infusion of 0.25 mg/kg/h. Target ACT of 180–220 s	Bivalirudin group had non-significantly higher rate of re-thoracotomy and non-significantly lower rates of delayed chest closure, stroke, intracranial bleeding, 30-day mortality, and 1-year mortality; PS matched analysis revealed no differences in significant outcomes
Pieri et al. [26]	12 adult pts undergoing LVAD placement; 10 pts due to dilated cardiomyopathy, 2 pts due to cardiogenic shock	Retrospective case series	No bivalirudin bolus reported; initial infusion rate 0.025 mg/kg/h; maintenance infusion rate of 0.04 mg/kg/h; target aPTT of 45–60 s	No thromboembolic or major bleeding complications; no VAD-related complications or hemolysis recorded; two episodes of minor bleeding from chest tubes that subsided after reduction or suspension of bivalirudin infusion; RBC transfusions required in 6 pts, FFP transfusion required in 1 pt; no platelet transfusions required; all pts survived to hospital discharge and 1 year; one pt died due to sepsis after 1.5 years of support
Bates et al. [25]	14 long-term VAD pts (9 adults, 5 pediatric) with 17 episodes of bivalirudin therapy; 13 episodes due to suspected or confirmed pump thrombosis, 1 episode due to HIT, 1 episode due to coagulopathy on UFH, 1 episode due to acute kidney injury, and 1 episode due to heparin resistance	Retrospective case series	No bivalirudin bolus reported; initial infusion rate 0.3 mg/kg/h; no maintenance dose reported, target aPTT of 70–90 or 80–100 s	Complications on bivalirudin: suspected pump thrombosis ($n = 2$); VAP ($n = 2$); major bleed, SDH secondary to fall ($n = 1$); GI bleeding ($n = 2$); hemorrhoids ($n = 1$). Outcome following discontinuation of bivalirudin: discharge on warfarin ($n = 8$); death ($n = 4$); transplant ($n = 3$); pump replaced ($n = 2$). No pt deaths directly related to bivalirudin; no reports of reaction to bivalirudin infusion or development of end-organ dysfunction
VanderPluym et al. [28]	43 pediatric pts on DTI for duration of VAD support (39 on bivalirudin); LVAD, $n = 28$; RVAD, $n = 2$; BiVAD, $n = 13$	Retrospective case series	No bivalirudin bolus reported; median initial infusion rate 0.3 mg/kg/h (range 0.1–1.4); median maximum dose 1.0 mg/kg/h (range 0.1–3.9). Target aPTT variable (range 50–100 s)	Major bleeding events occurred in 7 pts with 8 overall bleeding events (6 pts on bivalirudin, 1 on argatroban); all pts were on antiplatelet agent at time of bleeding event. Pump thrombosis event rate of 5.7 per 1000 pt days of support; neurologic event rate of 2.1 per 1000 pt days of support on bivalirudin
Campbell et al. [20]	19 pediatric pts on bivalirudin for VAD (9 pts with BiVAD, 5 pts with LVAD, 5 pts with RVAD)	Retrospective analysis	Initial median (IQR) infusion rate 0.1 (0.1–0.2) mg/kg/h; average infusion rate 0.4 (0.31–1) mg/kg/h; maximum median (IQR) infusion rate of 0.7 (0.41–1.2) mg/kg/h; target aPTT 60–90 s	Average percentage of time spent within goal aPTT range was 67.4%; higher average and maximum dose vs. pts on ECMO; similar initial dose used
Medar et al. [29]	11-month-old girl with dilated cardiomyopathy utilizing LVAD as bridge to transplant (122 days of support)	Case report	No bivalirudin bolus reported; initial infusion rate 0.15 mg/kg/h; maintenance rate ranged from 0.15 to 2.3 mg/kg/h; target aPTT 60–90 s	No evidence of thrombus or need for pump change, no significant bleeding intraoperatively or postoperatively. Pt discharged home on postoperative day 15

Taylor Am J CV Drugs 2020

Description of Bivalirudin Use for Anticoagulation in Pediatric Patients on Mechanical Circulatory Support

Christopher T. Campbell, PharmD[1,2], Lucas Diaz, PharmD[1], and Brian Kelly, PharmD[1]

Annals of Pharmacotherapy 00(0)

Table 1. Baseline Demographics.

Characteristic	VAD (n = 19)	ECMO (n = 15)	All (n = 34)
Age (years), median [IQR]	0.16 [0.019-9]	0.33 [0.0027-13]	0.29 [0.015-9.25]
Gender (male), n (%)	8 (42.1)	8 (53.3)	16 (47.1)
Weight (kg), median [IQR]	6.1 [4.4-28.1]	7.4 [3.3-23.7]	6.1 [3.9-24.8]
Height (cm), median [IQR]	67.3 [55.8-116.8]	65.9 [51-147]	66.6 [53.8-123.1]
BSA (m^2), median [IQR]	0.33 [0.26-0.95]	0.37 [0.21-0.98]	0.34 [0.24-0.96]
Primary service, n (%)			
PCICU	19 (100)	13 (86.6)	32 (94.1)
NICU	0 (0)	2 (13.4)	2 (5.9)
Baseline renal dysfunction, n (%)	2 (10.5)	0	2 (5.8)
Baseline hepatic dysfunction, n (%)	6 (31.5)	1 (6.6)	7 (20.5)
Primary cardiac comorbidity, n (%)	19 (100)	12 (80)	31 (91.1)
Cardiomyopathy	8 (42.1)	2 (13.3)	13 (38.2)
Congenital heart disease	6 (31.6)	7 (46.7)	10 (29.4)
Heart failure (unspecified)	3 (15.8)	2 (13.3)	5 (14.7)
Other	2 (10.5)	1 (6.7)	3 (8.8)

Table 2. Bivalirudin Dosing and Outcomes Between ECMO Versus VAD Patients.

Characteristic	VAD (n = 19)	ECMO (n = 15)	All (n = 34)	*P* value
Average dose (mg/kg/h), median [IQR]	0.4 [0.31-1]	0.28 [0.2-0.5]	0.37 [0.21-0.56]	0.044
Initial rate (mg/kg/h), median [IQR]	0.1 [0.1-0.2]	0.1 [0.05-0.18]	0.1 [0.5-0.2]	0.17
Maximum dose (mg/kg/h), median [IQR]	0.7 [0.41-1.2]	0.44 [0.22-0.66]	0.62 [0.33-0.91]	0.048
Duration of bivalirudin (days), median [IQR]	62.6 [12.9-120.8]	5.5 [4.5-7.5]	10.5 [5.2-88.5]	<0.01
Time to first therapeutic aPTT (hours)	5 [3-29]	6.5 [2.5-23]	6.1 [2.7-24.1]	0.65
Percentage time within therapeutic aPTT on bivalirudin, mean ± SD	67.4 ± 26.9	55 ± 29.5	61.9 ± 28.4	0.21

Campbell Annals of Pharmacotherapy 2021

Management of Hemostasis for Pediatric Patients on Ventricular-Assist Devices

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Jun Teruya, MD, DSc[2,3,4]

Semin Thromb Hemost. 2018 Feb

- **References**
- **All basic concepts**
- **Recent**

Adult and pediatric mechanical circulation: a guide for the hematologist

Lisa Baumann Kreuziger[1] and M. Patricia Massicotte[2] *Hematology 2018*

Table 1. MCS options for children and adults

Device	Type of flow	Max pump rate (max flow)	Used in children	Used in adults	Survival	Major hemorrhage	Ischemic stroke
Temporary							
VA-ECMO pumps[4]	Continuous	(10 L/min)	Yes	Yes	38-68% of ECLS	7-10%*,†	4%
Impella 2.5/CP/5.0[9,10]	Continuous	51 000 rpm (2.5 L/min); 46 000 rpm (4.0 L/min); 33 000 rpm (5.0 L/min)	Yes	Yes	25-46% at 1 mo (adults) 68% at 1 mo (pediatrics)	8% (adults) 5% (pediatrics)	4% (adults) 2% (pediatrics)
TandemHeart[8]	Continuous	3 000-7 000 rpm (5 L/min)	Yes	Yes	43-47% at 1 mo	42-90%	0%
Long-term							
EXCOR[14]	Pulsatile	30-120 bpm (3-7.2 L/min depending on pump size)	Yes	No	Median survival 144-174 d	28%-50%†,‡	6-29%
HeartMate II[6]	Continuous, axial	8 000-15 000 rpm (3-10 L/min)	Yes, adolescents	Yes	90% at 6 mo	14-15% at 6 mo	6% at 6 mo
HVAD[16]	Continuous, centrifugal	2 400-3 200 rpm (10 L/min)	Yes, adolescents	Yes	96% at 6 mo	10-14% at 6 mo	7% at 6 mo
HeartMate 3[6]	Continuous, centrifugal	3 000-9 000 rpm (10 L/min)	NR	Yes	91% at 6 mo	10-16% at 6 mo	5% at 6 mo
Syncardia TAH[12]	Pulsatile	125 bpm (7-9 L/min)	Yes, adolescents	Yes	68% to transplant	25% at 1 mo	5% at 1 mo

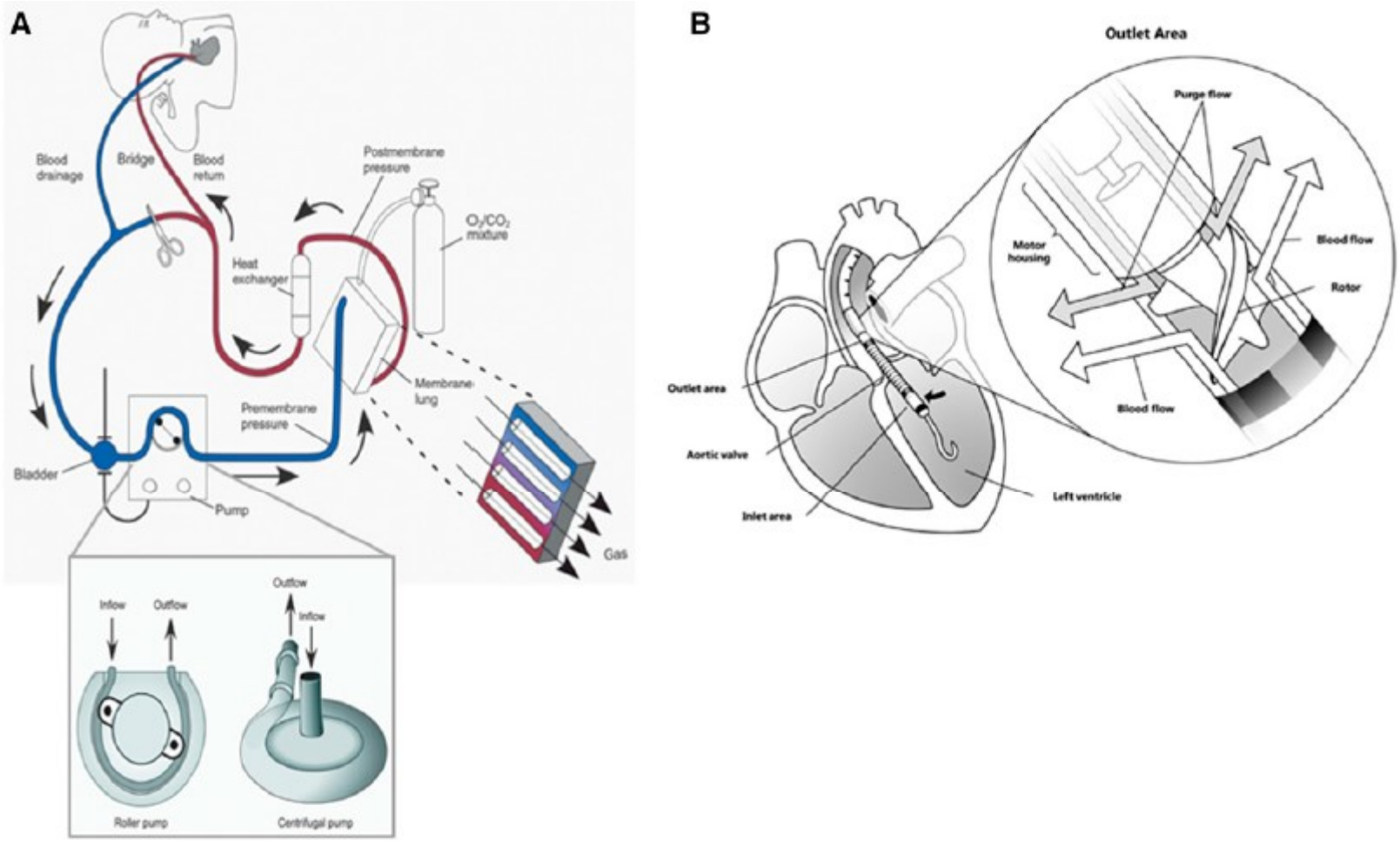

Figure 1. (A) Schematic of ECMO systems using a roller or centrifugal pump. Some centrifugal pumps can be used without the membrane lung as percutaneous VADs. (B) The Impella heart pumps are catheter-based temporary MCS devices. Purge fluid flows retrograde through the catheter in the femoral artery, past the motor housing to cool the rotor, and into the circulation. Originally published in Laliberte and Reed[11] © [2017], American Society of Health-System Pharmacists, Inc. All rights reserved. Reprinted with permission (R1804).

Kreuziger-Massicotte Hematology 2018

Table 2. Terminology used to describe MCS devices or indications for use

Term	Definition	Device examples
Description of device		
Extracorporeal	Pump for device located outside of the body	ECMO, CPB, EXCOR
Intracorporeal	Pump for device located with the body	HeartMate 3, HVAD
Temporary	Device intended for limited duration of support (hours-days)	Impella 2.5, Impella CP, ECMO
Durable	Device with capability of support for months-years	HeartMate 3, HVAD
Partial support	Device provides less flow than complete cardiac output	Impella 2.5
Full support	Device provides complete cardiac output	ECMO, EXCOR, HeartMate 3, HVAD
Dischargeable	Device does not require hospitalization for continued support	HeartMate 3, HVAD
Type of flow		
Pulsatile	Device with flexible membranes that creates intermittent flow and a pulse	Total artificial heart, EXCOR
Nonpulsatile/continuous flow	Device that provides constant blood flow	HeartMate 3, HVAD
Axial	Device with inlet and outflow in the same axis and flow produced by rotating impeller	HeartMate II, Jarvik 2000
Centrifugal	Device with inlet perpendicular to outflow tracts. Flow produced by centrifugal force.	HeartMate 3, HVAD
Indication for MCS use		
Bridge to transplant	Device implanted to support patient until a heart transplant	HeartMate II, HVAD
Bridge to candidacy	Device implanted to support patient until can determine whether eligible for a heart transplant	HeartMate II, HVAD
Bridge to recovery	Device implanted until myocardial recovery from injury	HeartMate II, HVAD
Destination therapy	Device implanted to support patients who are ineligible for heart transplant	HeartMate II, HVAD
Short term	New term to describe device implanted with intention for months-years of support (replaces bridge to transplant or recovery)	HeartMate 3
Long term	New term to describe device implanted with the intention for years of support (replaces destination therapy)	HeartMate II, HVAD

Kreuziger-Massicotte Hematology 2018

Table 3. Comparison between Edmonton antithrombotic guidelines and Stanford protocol for management of children with the Berlin Heart EXCOR pediatric VAD

	Edmonton protocol		Stanford protocol	
Medication	**Initiation parameters**	**Goal**	**Initiation parameters**	**Goal**
Perioperative				
Antithrombin concentrate or plasma	Antithrombin activity < 70%	Antithrombin activity ≥ 70%	Antithrombin activity < 70%	Antithrombin activity ≥ 70%
Protamine	Completion of CPB	Complete heparin reversal (institution-dependent parameters)	Completion of CBP	Complete heparin reversal (institution-dependent parameters)
Postoperative				
UFH	24 h postimplantation, platelets > 20 000/μL, normal TEG Platelet Mapping, TEG MAc_{KH} > 46 mm, TEG Rc_{KH} < 10	Anti-factor Xa 0.35-0.5 U/mL, TEG R 8.0-15.0	12-24 h postimplantation, platelets > 40 000/μL, no bleeding	Anti-factor Xa 0.35-0.5 U/mL
Antiplatelet				
Dipyridamole	48 h postimplantation, platelets > 40 000/μL, TEG MAc_{KH} > 56 mm, Platelet Mapping: net ADP G ≥ 4, AA inhibition < 70%	Platelet Mapping: net ADP G 4-8, AA inhibition > 70%	8 d after implant, add after max dose of asa reached and no bleeding	Titrated to a weight-based dose of 15 mg/kg/d
Aspirin	4 d postimplantation, TEG MAc_{KH} > 72 mm, net ADP G > 2	Platelet Mapping: net ADP G 4-8, AA inhibition > 70%	3 d postimplantation, no bleeding	Titrated to a weight-based dose of 30 mg/kg/d (max dose 2000 mg/d)
Clopidogrel	No recommendation		11 d postimplantation, after max dose of aspirin and dipyridamole reached and no bleeding	Titrated to weight-based dose of 0.2 mg/kg/d, max dose 1 mg/kg/d
Long-term anticoagulant				
Enoxaparin	Age < 1 y, >48 h postimplantation, normal creatinine	Anti-factor Xa 0.6-1.0 U/mL	Age ≤ 2 y, or if unstable INR	Anti-factor Xa 0.6-1.0 U/mL
Warfarin	Age ≥ 1 y, full oral diet	INR 2.7-3.5	Age > 2 y, full oral diet	INR 2.7-3.5
Anti-inflammatory				
Prednisone	No recommendation		As needed for fibrinogen > 600 mg/dL or other signs of inflammation (fever, rise in CRP), no other signs of sepsis	Methylprednisolone should be initiated at a dose of 2 mg/kg/d IV (or PO equivalent) divided BID, discontinue when fibrinogen ≤ 400 mg/dL

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PEDIMACS

Adverse events in children implanted with ventricular assist devices in the United States: Data from the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS)

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Robert L. Kormos, MD,[i] David C. Naftel, PhD,[g] Ryan J. Butts, MD,[j]
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Table 1 Major Adverse Events (With Brief Summary Description)

Adverse event	Brief description
Device malfunction	The device fails to perform as intended, can be major or minor
Major bleeding episode	Bleeding episode requiring transfusion, hospitalization or surgery, or resulting in death
Major infection	Clinical infection treated with an anti-microbial agent
Neurologic dysfunction	Temporary or permanent neurologic dysfunction or structural injury

Table 3 Adverse Event Incidence

	Number of events		
Event type	Pulsatile-flow VAD	Continuous-flow VAD	Total
Arterial non-CNS thromboembolism	0	2	2
Bleeding	31	37	68
Cardiac arrhythmia	9	17	26
Device malfunction	63	16	79
Hepatic dysfunction	3	4	7
Infection	38	40	78
Pump-related, including drive-line	(8)	(6)	(14)
Bloodstream/sepsis	(13)	(10)	(23)
Pulmonary	(7)	(9)	(16)
Other	(10)	(15)	(25)
Neurologic dysfunction	41	11	52
Ischemic stroke	(10)	(1)	(11)
Hemorrhagic stroke	(8)	(1)	(9)
Other	(23)	(9)	(32)
Other SAE	22	18	40
Pericardial drainage	4	9	13
Psychiatric episode	1	9	10
Renal dysfunction	8	7	15
Respiratory failure	12	14	26
Venous thromboembolism	0	1	1
Wound dehiscence	0	1	1
Total	232	186	418

CNS, central nervous system; SAE, serious adverse event; VAD, ventricular assist device; ( ) signify number of events in a subcategory.

Antiaggregants et EI

Outcomes of pediatric patients supported with continuous-flow ventricular assist devices: A report from the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS)

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The Journal of Heart and Lung Transplantation, Vol 35, No 5, May 2016

- IC
- Etude 2016 enfants vs adultes 2012-2015
- Enfants très bonne outcome mais saignement 37/109 EI 16/109 11/109 AVC

Thrombosis Research 172 (2018) 194–203

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Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

Antithrombotic therapies in children on durable Ventricular Assist Devices: A literature review

Joanna Y. Huang[a,b,c], Paul Monagle[b,c,d,*], M. Patricia Massicotte[e], Christina J. VanderPluym[f]

Definition of bleeding and clotting events differed between cohorts. The incidence of bleeding overall was 37% (209/558; range of 0 to 89%) and 26% (143/554; range of 8.3 to 100%) for thromboembolism events. All studies reported had significant methodological limitations.

Conclusions: The clinical use of antithrombotic therapies – including dosages, timing and monitoring – varies considerably. This review highlights the further research required to improve understanding of hemostasis in the pediatric VAD field.

Complications

Adverse Events in Children Implanted with Ventricular Assist Devices in the US: Data from the Pediatric Interagency Registry for Mechanical Circulatory Support (Pedimacs)

DN Rosenthal[1], CS Almond[1], RD Jaquiss[2], CE Peyton[3], SR Auerbach[4], DL Morales[5], DJ Epstein[6], RS Cantor[7,8], RL Kormos[9], DC Naftel[7], RJ Butts[10], NS Ghanayem[11], JK Kirklin[7], and ED Blume[12]

J Heart Lung Transplant. 2016 May ; 35(5): 569–577

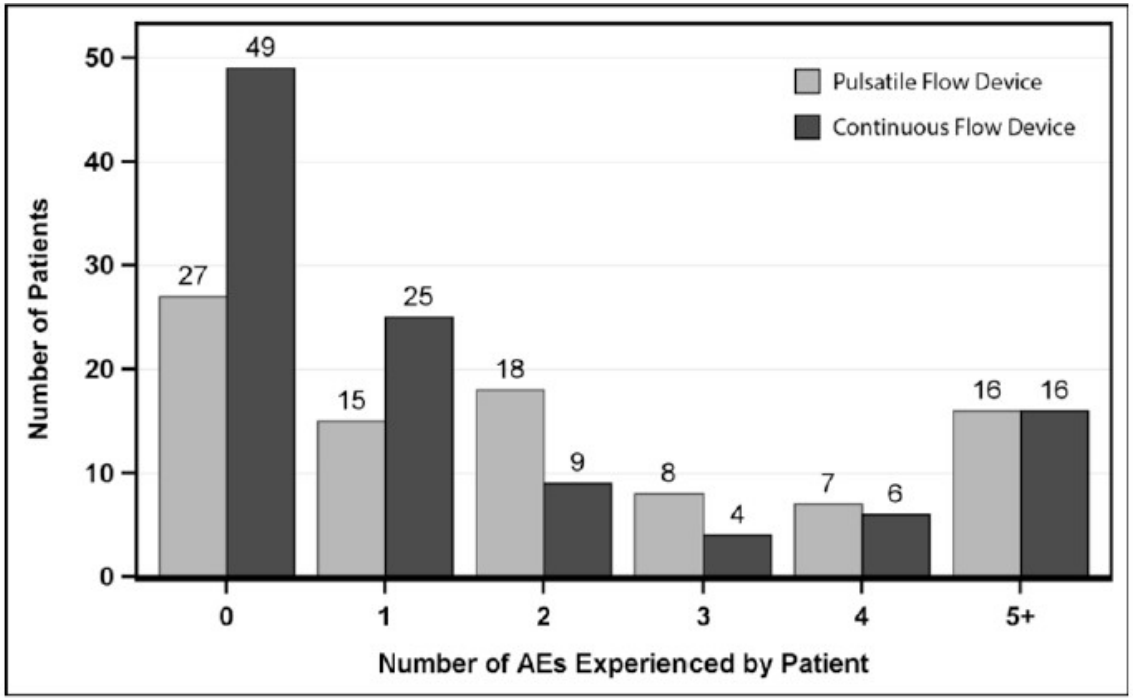

Figure 1. Number of Adverse Events per Patient
Pedimacs patients receiving durable implants, Sept 2012 to Aug 2015 (patients=200)

Principaux évenements indesirables

Adverse Event	Brief description
Device Malfunction	The device fails to perform as intended, can be major or minor
Major Bleeding Episode	Bleeding episode requiring transfusion, hospitalization, or surgery; or resulting in death
Major Infection	Clinical infection treated with an anti-microbial agent
Neurological Dysfuction	Temporary or permanent neurological dysfunction or structural injury

Differences clinique pulsatile vs continous VAD

	Pulsatile flow (n=91)	Continuous flow (n=109)	P-value
Age (yr)	4.6 +/- 5.0	14.4 +/- 3.7	<.0001
Female	42 (46.2)	36 (33.0)	0.0581
Cardiac diagnosis			
Cardiomyopathy	56 (61.5)	90 (82.6)	
Myocarditis	10 (11.0)	7 (6.4)	
Congenital Heart disease	24 (26.4)	11 (10.1)	
Other	1 (1.1)	1 (0.9)	
Race			0.6849
Caucasian	56 (61.5)	64 (58.7)	
African-American	35 (38.5)	45 (41.3)	
BSA m2	0.7 +/- 0.5	1.7 +/- 0.4	<.0001
Prior Cardiac Surgery	50 (54.9)	26 (23.9)	<.0001
Prior ECMO	22 (24.2)	8 (7.3)	0.0009
Intermacs Level			0.0139
I (critical cardiogenic shock)	32 (36.8)	20 (19.0)	
II (progressive decline on inotropes)	43 (49.4)	64 (61.0)	
III (stable, but inotrope dependent)	7 (8.0)	18 (17.1)	
IV (resting symptoms)	5 (5.7)	3 (2.9)	
Pre-Implant Device Strategy			0.0068
Bridge to Transplant - Listed	69 (75.8)	59 (54.1)	
Bridge to Candidacy	19 (20.9)	44 (40.4)	
Destination Therapy	2 (2.2)	6 (5.5)	
Bridge to Recovery	1 (1.1)	0 (0.0)	
Implant Device Type			0.0068
LVAD	59 (64.8)	102 (93.6)	
RVAD	3 (3.3)	1 (0.9)	
BiVAD	23 (25.3)	6 (5.5)	
TAH	6 (6.6)	0 (0.0)	
Selected Laboratory Values			
Sodium (mEq/L)	138.2 +/- 5.8	136.3 +/- 6.3	0.0254
Blood Urea Nitrogen (mg/dL)	30.2 +/- 22.4	24.5 +/- 15.0	0.032
Creatinine (mg/dL)	0.6 +/- 0.5	1.0 +/- 0.5	<.0001
Brain Natriuretic Peptide (pg/mL)	2488.6 +/- 1890.6	1641.3 +/- 1460.3	0.0156
Pro Brain Natriuretic Peptide (pg/mL)	17721 +/- 14991	8891.7 +/- 9157.8	0.0136
Albumin (g/dL)	3.5 +/- 0.8	3.5 +/- 0.5	0.4292
NR	1.4 +/- 0.5	1.5 +/- 0.6	0.8349

Fréquence EI

200 pts, 418 EI, précoce vs tard (90 jours)

P ≠ C drainage péricardique

Enfants < Adultes
Plus frequents: device malfunction (79), infection (78), neurological dysfunction (52) bleeding (68)

Ensemble 277 EI, 66% du total. 38% pas EI, 16% of > 5 EI

Adverse Event Incidence

	Number of Events		
Event Type	Pulsatile Flow VAD	Continuous Flow VAD	Total
Arterial Non-CNS Thromboembolism	0	2	2
Bleeding	31	37	68
Cardiac Arrhythmia	9	17	26
Device Malfunction	63	16	79
Hepatic Dysfunction	3	4	7
Infection	38	40	78
Pump related, including driveline	(8)	(6)	(14)
Bloodstream/Sepsis	(13)	(10)	(23)
Pulmonary	(7)	(9)	(16)
Other	(10)	(15)	(25)
Neurological Dysfunction	41	11	52
Ischemic Stroke	(10)	(1)	(11)
Hemorrhagic Stroke	(8)	(1)	(9)
Other	(23)	(9)	(32)
Other SAE	22	18	40
Pericardial Drainage	4	9	13
Psychiatric Episode	1	9	10
Renal Dysfunction	8	7	15
Respiratory Failure	12	14	26
Venous Thromboembolism	0	1	1
Wound Dehiscence	0	1	1
Total	232	186	418

Antithrombosis Harmonization Protocol for Pulsatile Paracorporeal VADs (Berlin Heart EXCOR)

action
ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

BIVALIRUDIN

1. **Pre-VAD implantation work-up (<48 hours pre VAD/MCS):**
   - Baseline labs: CBC with diff, aPTT*, PT/INR, fibrinogen, basic metabolic panel (BMP)
   - Optional labs: TEG with PM, CRP, LDH, cystatin C, HIT screen, ROTEM
2. **Intra-op management**
   - Standard heparin anticoagulation for cardiopulmonary bypass with full protamine reversal in OR
   - Standard blood product replacement to normalize coagulation parameters and establish hemostasis in OR
3. **Early post-op management**
   - Labs (aPTT, PT/INR, fibrinogen, BMP, CBC) within 2 hours of arrival to ICU
   - Optional: dilute thrombin time (dTT), TEG ± PM, ROTEM
   - It appears reasonable to start bivalirudin once:
     - Surgical and coagulopathic bleeding resolved (< 2 ml/kg of chest tube output for 4 hours and no other sources of active bleeding)
     - aPTT within 15 sec of baseline* (or institutional normative range)
     - INR <1.3
     - Fibrinogen > 200
     - Platelet count >100,000
   - Correct with blood product replacement as needed, being mindful of risk of dilutional coagulopathy with multiple PRBC transfusions, and correct any surgical bleeding as needed

Standard Goals: In order to learn more about what the ideal level of bivalirudin anticoagulation is, suggested standard goals based on national data have been set as a suggestion. This also helps with clarity for teams at the bedside. Not only are their goal ranges but target PTTs that are central to the range so that patients with a PTT of 61 when the goal is 60-80 will be managed so time within a goal range could possibly be higher.

Antithrombosis Harmonization Protocol for Pulsatile Paracorporeal VADs (Berlin Heart EXCOR)

action
ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

- **Early Post-op (24-72 hours, high risk for bleeding) target aPTT 55 (goal range 50-60)**
- **Maintenance (standard risk for bleeding) target aPTT 70 (goal range 60-80)**
- **Maintenance (High risk for thrombosis) target aPTT 80(goal range 70-90)**

TABLE 1: Initial Bivalirudin Dosing	
Goal: aPTT • *High risk (of bleeding): aPTT 50-60 sec*	**Goal: dilute thrombin time (dTT)** • *High risk (of bleeding): dTT 50-60 sec*
Renal function (GFR)	Initial dosing
Normal (>60ml/min/1.73 m2)	0.3 mg/kg/hr IV infusion
Mild-moderate (30-60ml/min/1.73 m2)	0.2 mg/kg/hr IV infusion
Severe (<30ml/min/1.73 m2)	0.1 mg/kg/hr IV infusion

- Check aPTT 2 hours after first initiation. Cautious about titrating with first level.
  - If aPTT has jumped dramatically to >2-3 x baseline PTT, then decrease Bival by 50% and recheck in 2-3 hours
  - If PTT has increased to 1-1.5 x baseline, make no adjustment and repeat PTT in 2-3 hours as level may continue to rise

Antithrombosis Harmonization Protocol for Pulsatile Paracorporeal VADs (Berlin Heart EXCOR)

action
ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

This document is intended to provide recommendations for antithrombosis management of pulsatile paracorporeal VADs (Berlin Heart EXCOR) in children. It was created through the sharing of experience, expertise and data of the ACTION learning collaborative.

TABLE 2: Maintenance Bivalirudin titration

Goal: aPTT	**Goal: dTT**
• *Standard risk: aPTT 60-80 sec* • *High risk (of thrombosis): aPTT 70-90 sec*	• *Standard risk: dTT 60-80 sec* • *High risk (of thrombosis): dTT 70-90 sec*
If aPTT 5 to 15 sec out of range: • Increase or decrease by 15% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change	***If dTT 5 to 15 sec out of range:*** • Increase or decrease by 15% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change
If aPTT in target range, no change. • Recheck 2-3 hrs., then can decrease frequency when stable	***If dTT is in target range, no change:*** • Recheck 2-3 hrs., then can decrease frequency when stable
If aPTT ≥15-30 sec out of range • Increase or decrease by 25% (round up to closest 2nd decimal • Recheck 2-3 hours after dose change	***If dTT ≥15-30 sec out of range:*** • Increase or decrease by 25% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change
If aPTT >3x baseline or ~120 sec: • With normal renal function: hold 15 min and reduce by 30% • With mild to moderate renal dysfunction: hold for 45 min and reduce by 40% • With severe renal dysfunction: hold 2 hours and recheck PTT before restarting	***If dTT >100sec:*** • With normal renal function: hold 15 min and reduce by 30% • With mild to moderate renal dysfunction: hold for 45 min and reduce by 40% • With severe renal dysfunction: hold 2 hours and recheck PTT before restarting

SIMPLE TITRATION RULE: Adjust your bivalirudin infusion the same % as the difference between the current aPTT and goal aPTT you are trying to achieve

NOTE:

- **aPTT may be impacted with the following:**
  - heparin contamination (from line) (↑aPTT)** (can use concomitant anti-XA (HAL) and/or INR/PT to identify contamination, since INR/PT will NOT increase with heparin contamination alone, BUT will increase with bival concentration)
  - traumatic phlebotomy, high pressure exerted on syringe during sampling (↑aPTT)
  - Stasis draw - either from a sluggish IV for a lab that sat in the lab for too long can be falsely low
  - low fibrinogen, low FXII, VIII (>30-40% depletion) (Example: chylous effusion, excessive PD drainage, liver dysfunction, consumption within clot) (↑aPTT)
  - plateau aPTT: may be seen at high concentrations of bivalirudin (>1mg/L), consider using PT/INR and/or dTT, or DTI specific assay ecarin TT(Hemoclot, HemosIL DTI) [Stago, or STA-R Evolution]

- **dTT may be impacted by the following:**
  - heparin contamination (from line) (↑dTT)** (can use concomitant INR/PT to identify contamination, since INR/PT will NOT increase with heparin contamination alone, BUT will increase with bival concentration)
  - fibrinogen levels
  - NOT impacted by lupus inhibitors or elevated d-dimer
  - Stasis draw - either from a sluggish IV for a lab that sat in the lab for too long can be falsely low

ARGATROBAN

- Partial hepatic metabolism: no need to dose based on renal dysfunction
- If your hepatic function changes, then you should re-check your levels and titrate more cautiously
- Half-life: 39-51 min, may be prolonged further with hepatic dysfunction

The recommended starting dose of Argatroban is 0.5 mcg/kg/min.

- **Titration increments are typically 0.2-0.5 mcg/kg/min with final therapeutic doses typically between 1-5 mcg/kg/min.**
- **Doses as high as 5-8 mcg/kg/min have been used with the recommended maximum in the adult literature of 10 mcg/kg/min.**

TABLE 3: Initial Argatroban Dosing:	
Goal: aPTT • *High risk (of bleeding): aPTT 50-60 sec*	**Goal: dilute thrombin time (dTT)** • *High risk (of bleeding): dTT 50-60 sec*
Initial dosing: 0.5 mg/kg/min IV infusion - consider lower dosing if know hepatic dysfunction with baseline elevated INR	

ARGATROBAN

TABLE 4: Maintenance Argatroban titration	
Goal: aPTT • *Standard risk: aPTT 60-80 sec* • *High risk (of thrombosis): aPTT 70-90 sec*	**Goal: dTT** • *Standard risk: dTT 60-80 sec* • *High risk (of thrombosis): dTT 70-90 sec*
If aPTT 5 to 15 sec out of range: • Increase or decrease by 15% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change	***If dTT 5 to 10 sec out of range:*** • Increase or decrease by 15% (round up to closest 2nd decimal) • Recheck 2-3 hours after dose change
If aPTT in target range, no change. • Recheck 2-3 hrs., then daily after 2 consecutive in range values	***If dTT is in target range, no change:*** • Recheck 2-3 hrs., then daily after 2 consecutive in range values

TRANSITION FROM DTI TO VITAMIN K ANTAGONIST (VKA)

- Patients may remain on the DTI for the duration of VAD support, or can be transitioned to enteral VKA at the discretion of the care time
- NOTE: potential for combined effects on INR with co-administration of bivalirudin and warfarin therefore a loading dose of warfarin should NOT be used
- Obtain baseline INR on bivalirudin therapy (NOTE: INR will be prolonged with bivalirudin alone)
- Initiate warfarin at 0.1-0.2 mg/kg/day and obtain daily INR
- Bivalirudin can be discontinued once INR >1.5 above baseline INR (example: if baseline INR 2 on bivalirudin, then discontinue bivalirudin once INR 3.5 on combined bivalirudin and warfarin)
- Target INR for warfarin therapy alone:3-4
- Bivalirudin should be resumed if INR <3

TRANSITION FROM DTI TO LOW MOELCULAR WEIGHT HEPARIN (Enoxaparin)

- Patients may remain on the DTI for the duration of VAD support, or can be transitioned to subcutaneous LMWH at the discretion of the care time
- Bivalirudin should be discontinued 2 hours after administration of enoxaparin dose and dosed as per institutional recommendations for therapeutic dosing as follows:
  - <37 weeks GA and <3 months: 2 mg/kg/dose sc q 12h
  - ≥ 37 weeks GA and <3 months: 1.7 mg/kg/dose sc q 12 h
  - ≥ 3 months-12 months: 1.5 mg/kg/dose sc q 12 h
  - ≥ 12 months: 1 mg/kg/dose sc q 12 h
- Target LMWH level (anti-Xa level) 0.8-1.2
  - If concern for high risk of thrombosis: target anti-Xa 1-1.5
  - If concern for high than standard risk of bleeding: target anti-Xa 0.5-0.8 OR transition back to bivalirudin for closer titration of anticoagulation goals

Acquired von Willebrand Syndrome in Patients With Ventricular Assist Device

Frontiers in Medicine
February 2019 | Volume 6 | Article 7

Antoine Rauch [1,2], Sophie Susen [1,3*] and Barbara Zieger [3]

Mechanism

AVWS develops due to Increased shear stress caused by the VAD
→Loss of the HMW-multimers
→ Reduced VWF collagen binding activity (VWF:CB), ristocetin cofactor activity (VWF:RCo), and VWF:Activity (VWF:Ac)
→ Reduction of the corresponding VWF:CB/VWFAntigen(VWF:CB/VWF:Ag)-ratio, VWF:RCo/VWF-Antigen (VWF:RCo/VWF:Ag)-ratio, and VWF:Act/VWF-Antigen (VWF:Ac/VWF:Ag)-ratios
→ VWF:CB and VWF:RCo-factor, decreased in VAD-patients

- All the CF-VAD patients presented a loss of the VWFHMW-multimers = AVWS
- Heilmann et al. CF-VAD patients developed AVWS within 1 day
- Further investigations, acquired VWF defect within 3 h after VAD-implantation and totally reversed after
CF-VAD weaning

Rauch Font in Med 2019

CLINICAL IMPLICATIONS OF AVWS IN VAD-PATIENTS: 1) Perioperative bleeding 2) Mucosale bleeding (Princ. GI)

PATHOPHYSIOLOGY OF BLEEDING RELATED TO AVWS IN VAD-PATIENTS: arteriovenous malformations (AVM) in gastrointestinal and nasal tracts. Neo-angiogenesis. Angiodysplasia.

TABLE 1 | Published Literature on the management of GI-bleeding in LVAD patients with antiangiogenic drugs or VWF concentrate.

Authors	Patients treated	Indication	Medication	Outcome	Adverse events
Loyaga-Rendon et al. (70)	7	Secondary prophylaxis of GI-bleeding	Octreotide	No significant reduction in hospitalizations, transfusion need, or number of endoscopies at 3 months	Abdominal pain Diarrhea
Aggarwal et al. (71)	10	Secondary prophylaxis of GI-bleeding	Secondary prophylaxis	No difference in length of hospitalization, GIB recurrence rate, or transfusion need	None reported
Hayes et al. (72)	5	Secondary prophylaxis of GI-bleeding	Octreotide	Successfully treated	None reported
Malhotra et al. (73)	10	Primary prophylaxis of GI-bleeding	Octreotide	No GI-Bleeding events	None reported
Shah et al. (52)	51	Secondary prophylaxis of GI-bleeding	Octreotide	Lower recurrence of GI bleed compared to a matched historical control group (24 vs. 43%; $p = 0.04$)	None reported
Draper et al. (74)	8	Secondary prophylaxis of GI-bleeding	Thalidomide	5 patients had no recurrence of bleeding 2 patients had reduction of bleeding 1 patient died within 1 week of initiation	Neuropathy, Sepsis
Ray et al. (75)	1	Secondary prophylaxis of GI-bleeding	Thalidomide	No recurrent bleeding at 1 year	No thrombosis at 1 year
Seng et al. (76)	11	Secondary prophylaxis of GI-bleeding	Thalidomide	Recurrent GIB occurred in 4 patients (45.4%) post-discontinuation of thalidomide therapy	1 pump thrombosis 1 Neuropathy
Fischer et al. (77)	1	Refractory GI-bleeding	VWF concentrate 80 IU/kg daily	1st GI-bleeding event successfully treated. Restart of VWF therapy with octreotide after recurrence of GI-bleeding	No thrombosis

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Hémorragie

- SNC : AVC hémorragique , évolution hémorragique AVC ischémique. Autres: GI, RESPIRATOIRE, site opératoire

- Précoce : essentiel régler problèmes hémostase chirurgicale < 6-12H

- Tardive : 50% pour protocole (avant changements)

Hémorragie

TAXI et PALISI

Pediatr Crit Care Med. 2018 September ; 19(9): S157–S162. doi:10.1097/PCC.0000000000001600.

Recommendations on the Indications for Red Blood Cell Transfusion for the Critically Ill Child Receiving Support from Extracorporeal Membrane Oxygenation, Ventricular Assist, and Renal Replacement Therapy Devices from the Pediatric Critical Care Transfusion and Anemia Expertise Initiative

Melania M. Bembea, MD, PhD[1], Ira M. Cheifetz, MD[2], James Fortenberry, MD[3], Timothy Bunchman, MD[4], Stacey Valentine, MD MPH[5], Scot Bateman, MD[5], Marie Steiner, MD, MS[6], and for the Pediatric Critical Care Transfusion and Anemia Expertise Initiative (TAXI) *, in collaboration with the Pediatric Critical Care Blood Research Network (BloodNet), and the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network

Hémorragie

TAXI et PALISI

- **Transfusion pour garder setting preop**
- **Optimiser taux Hb pour optimiser DaO2**
- **Grosses différences pour les pratiques entre centres**
- **Pas évidences de transfuser si pas d'hémorragie**
- **Augmentation morbidité-mortalité**
- **Recommandations gestion clinique et recherche**

Hémorragie TAXI et PALISI

Gestion clinique

1) <u>Targets and red flags</u>

- Choisir target Hb + paramètres physiologiques + biomarkers VO2 et DaO2
- Attention sensibilisation ABO et risque développer Ac anti-HLA augmenté par transfusion
- Transfuser que pts symptomatiques

2) <u>CRRT</u>

- Circuits sur < 20 kgs (NIDUS, CARPEDIEM, mini-circuits-Japon) ; priming ; volume/diluition
- Synthèse EPO
- Hémolyse

Hémorragie TAXI et PALISI

Recherche

1. DaO2-markers VO2 (ScVO2, NIRS cérébrale, NIRS rénale, oxymétrie régionale) (*Microcirculation ?)*
2. Corrélation transfusion avec allo-immunitation (Ac anti-HLA), risque perte de chance greffons compatibles, risque rejet
3. Critères conservation, manipulation, attribution (Irradiation, leuko-depletion, recherche CMV-EBV, recherche AG mineurs, lavage CGR, PFC, filtration, âge de la poche)
4. CRRT, dialyse

Hémorragie

- Diagnostic : chirurgicale ou médicale ? (Précoce)
- LABO standard vs POC hémostase (TEG, ROTEM)
- Bedside vs integration ICU-labo hémato (*Baumann Kreuziger and Massicotte, Hematology 2018*)

Dans le cadre de tests TEG-ROTEM-LABO altérés :

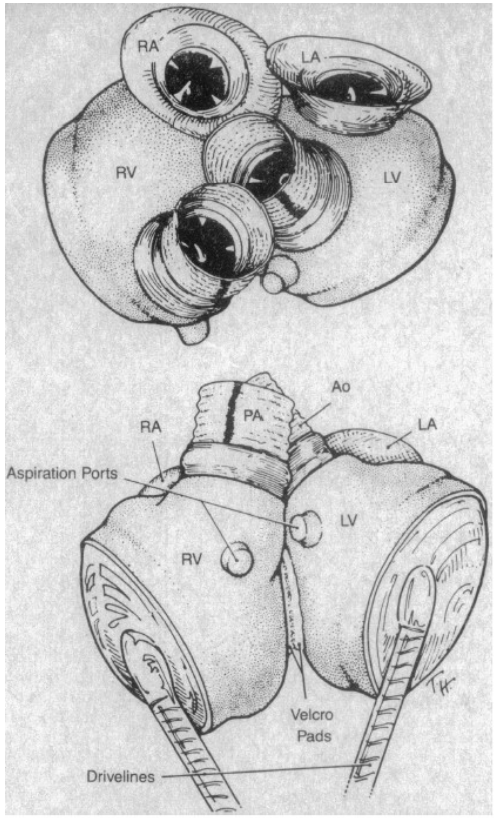
- ❑ Protamine sulphate PO immédiat si ACT > 150 sec or RK TEG > 16 min
- ❑ PFC 15-20ml/kg ou PCCs (Confidex) 25 UI/kg hours si TP 70 % (Répeter entre 8-12H si besoin)
- ❑ Fibrinogène 50 mg/kg si FGN < 1.5 g/L
- ❑ Plaquettes 1 UP/5-8 kg si PLT count < 50000 10^3 u/L or MA TEG < 45 mm (TEG)
- ❑ SI AVK préimplantation (Warfarin) : Vit K 2.5 -5.0 mg/J pour 3 jours

Jarvik

Surgical Technique for Implantation of the Jarvik-7-100 Total Artificial Heart

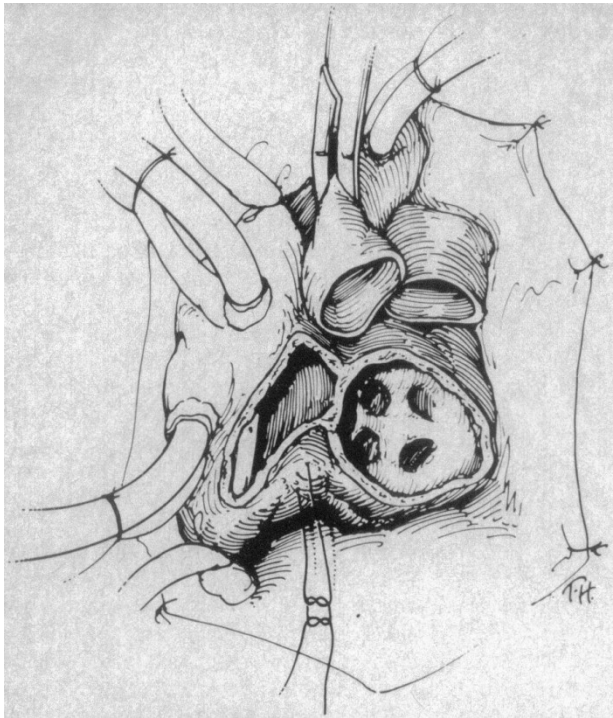
William C. DeVries, MD

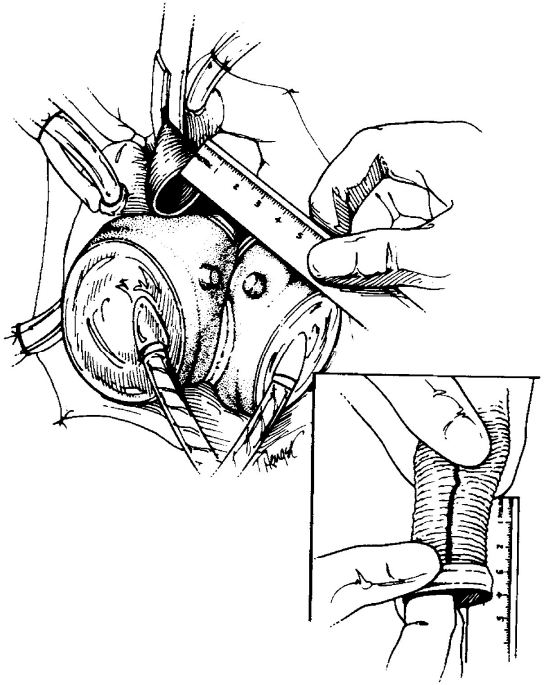
JAMA, Feb 12, 1988—Vol 259, No. 6

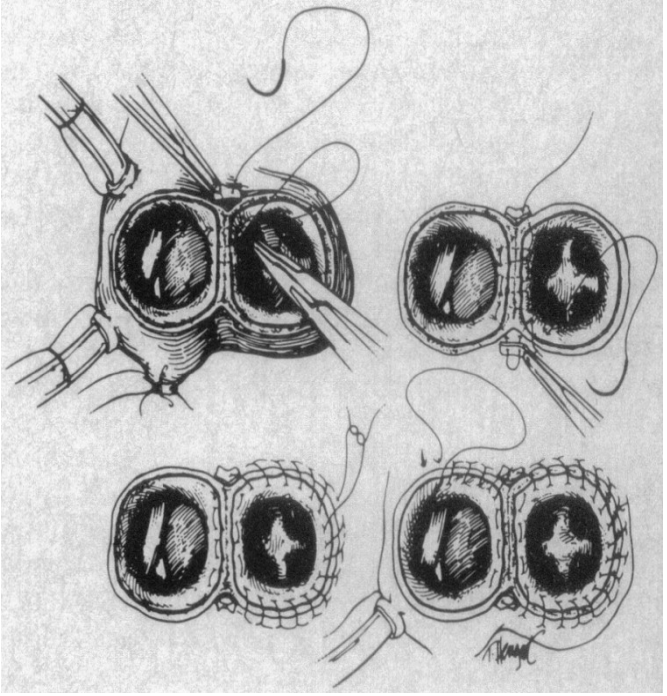


The Jarvik-7-100 total artificial heart is a pneumatically powered right and left ventricle replacement device. The device weighs 480 g, measures approxi¬ mately 10 x 10 x 15 cm, and is made of polyurethane (Fig 1). Blood is pumped by the action of a pulsed air-activated diaphragm with unidirectional blood flow obtained by the use of clinical grade valves (Medtronic-Hall, Medtronic, Ine, Minneapolis) (Fig l).10·

Jarvik







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Jarvik

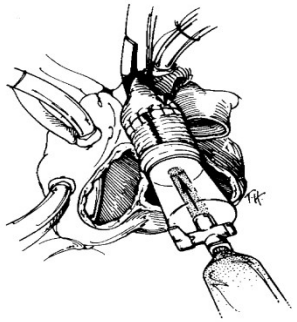

Fig 7.—Hemostasis of each anastomosis is tested by manual injection of blood via adapted syringe fitted to each graft's quick-connect cuff.

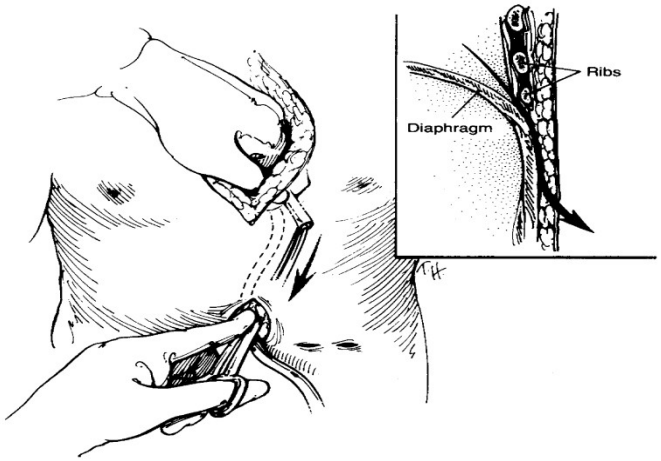

Fig 8.—Before insertion of left ventricle, pneumatic drive line is tunneled from thoracic cavity, through abdominal musculature to ribs, and then through subcutaneous pocket, exiting to skin at midline abdominal incision. Inset, Close-up view.

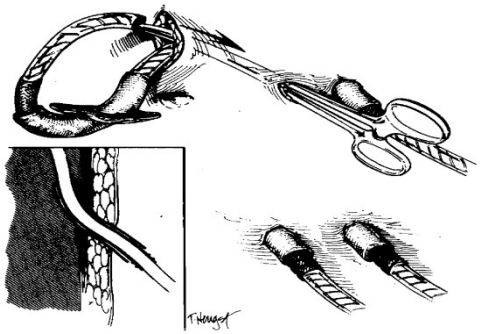

Fig 9.—Skin button is then attached by slipping onto drive lines. Flange is pulled back on itself to form intussusception (inset). End of drive lines will then be brought out through skin with flange of skin button lying flat in subdermal layer.

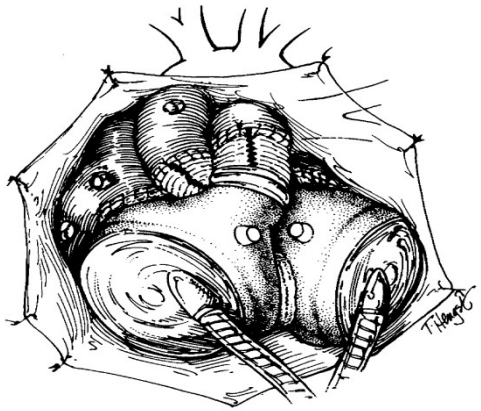

Fig 10.—Using ventricular aspiration ports on blood chambers of ventricles, air is removed from each ventricle before priming with blood and initiation of pumping via Utahdrive System (Symbion, Inc, Salt Lake City).

Surgical Technique for Implantation of the Jarvik-7-100 Total Artificial Heart

William C. DeVries, MD

Jarvik

Avantages Continuos Axial Flow VAD

- Pas de « réservoir » de sang (Zone à risque de thrombose et lésions cellulaires)
- Interface sang- VAD réduite
- Pas de valves artificielles (B-H)
- Mouvement unidirectionnel du sang → < risque usure
- < consumation d' énergie (Autonomie batterie B-H Excor max 30 min)
- Poids et dimensions petits
- Pratiquement pas de bruits (Excor !!!)
- < taux infections
- < taux dysfonction pompe

Jarvik

Research and Development of an Implantable, Axial-Flow Left Ventricular Assist Device: The Jarvik 2000 Heart

(Ann Thorac Surg 2001;71:S125–32)

O. H. Frazier, MD, Timothy J. Myers, BS, Robert K. Jarvik, MD, Stephen Westaby, FRCS, David W. Pigott, FRCA, Igor D. Gregoric, MD, Tehreen Khan, MD, Daniel W. Tamez, BS, Jeff L. Conger, BS, and Michael P. Macris, MD

Cullen Cardiovascular Surgical Research Laboratories, Texas Heart Institute, Houston, Texas, Jarvik Heart, Inc, New York, New York, and Oxford Heart Centre, Oxford, England

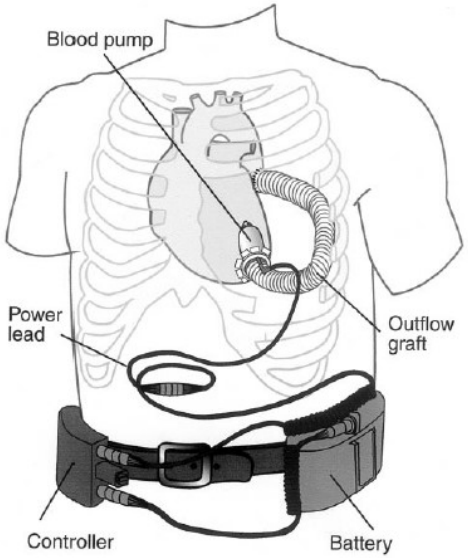

Fig 2. Percutaneous version of the Jarvik 2000. The blood pump is placed within the left ventricle, and the outflow graft is attached to the descending thoracic aorta. The percutaneous lead passes through the abdominal wall and is connected to an external control unit. Power for the implanted pump is received from a battery connected to the controller. (Reprinted from Myers and associates [13] with permission, Isis Medical Media Ltd, Oxford, UK.)

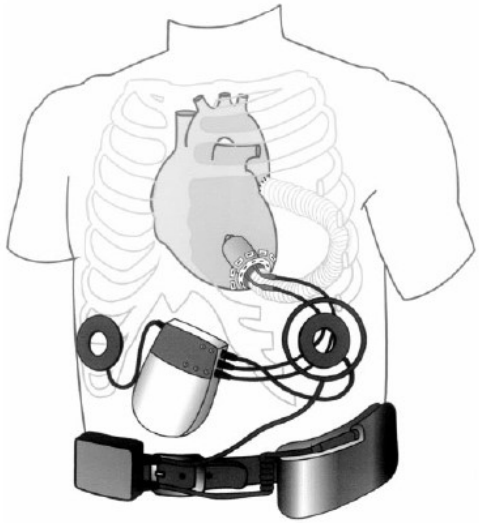

Fig 3. Totally implantable version of the Jarvik 2000. Two power leads exit from the blood pump and are connected to the internal power and control unit. Primary and secondary transcutaneous energy transmission systems coils are placed in different locations in the abdominal wall. The primary transcutaneous energy transmission systems coil provides external power and control, and the secondary transcutaneous energy transmission systems coil allows backup operation. (Reprinted from Myers and associates [13] with permission, Isis Medical Media Ltd, Oxford, UK.)

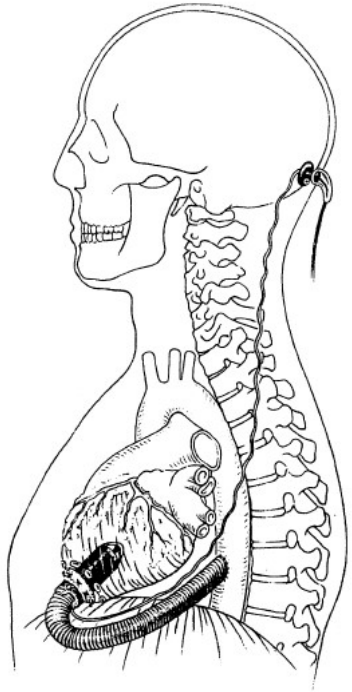

Fig 4. A third version of the Jarvik 2000 system incorporates a t nium pedestal mounted to the posterior portion of the skull. The power and control connection is made just outside the skin. (Reprinted from Westaby and coworkers [15] with permission.)

Jarvik

Advances in technology + increased clinical → development of a new type of blood pump

Jarvik 2000 Heart: electrically powered, axial-flow left ventricular assist device developed in 13 years

Unlike first-generation left ventricular assist devices, 1970s and designed to totally capture the CO, Jarvik 2000 designed to normalize the CO by augmenting the function of the chronically failed heart for extended periods…

Interactions tested in 67 animals, and ... Three patients have received the Jarvik 2000 as a bridge to transplantation, and 1 patient is being supported permanently outside the hospital. All 4 patients have improved from NYHA functional class IV to class I, and 2 of them have been discharged from the hospital after HT

The experimental and clinical results indicate that the Jarvik 2000 can provide physiologic support → minimal complications, reliable, biocompatible,easy to implant

Jarvik

↓

Jarvik 2000

↓

Infant Jarvik 2000

↓

Pumps for KIDS, Infants and Neonates (PumpKIN)

↓

Jarvik 2015 VAD

Jarvik

Années 2000-2010

Le problème principale dans le milieu MCS au niveau mondiale ? Absence dispositifs appropriés conçus pour traiter les problèmes anatomiques et besoins physiologiques des enfants

US federal government financement pour le Pediatric Circulatory Support Program of the National Heart, Lung and Blood Institute (NHLBI)

Projet- réalisation de 5 dispositifs d'assistance ventriculaire miniaturisés pour les nourrissons et enfants 2 - 25 kg atteints d'une maladie cardiovasculaire congénitale ou acquise

1) Duncan BW. *Pediatric mechanical circulatory support in the United States: past, present, and future.* ASAIO J. 2006 Sep-Oct;52(5):525-9. Review

2) Baldwin JT et al. *The National Heart, Lung, and Blood Institute Pediatric Circulatory Support Program.* Circulation 2006;113: 147–155

3) Wearden PD et al. *The PediaFlow pediatric ventricular assist device.* Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu 2006; 9: 92–98

4) Duncan BW et al. *The pedipump: development status of a new pediatric ventricular assist device.* ASAIO J 2005; 51: 536–539

4) Duncan BW et al. *The PediPump: a new ventricular assist device for children.* Artif Organs 29: 527–530, 2005

6) Weiss WJ. *Pulsatile pediatric ventricular assist devices.* ASAIO J 51: 540–545, 2005

7) Morales DL et al. *Lessons learned from the first application of the DeBakey VAD Child: an intracorporeal ventricular assist device for children.* J Heart Lung Transplant. 2005 Mar;24(3):331

Pumps for KIDS, Infants and Neonates (PumpKIN)

Janvier 2010

(1) PediaFlow VAD - an implantable, magnetically suspended, mixed-flow turbo-dynamic VAD, designed for children up to 2 years of age (University of Pittsburg with World Heart Inc.)
(2) Pediatric Pump Lung (PediPL) - an implantable, mixed-flow VAD with a magnetically suspended impeller (University of Maryland with Levitronix LLC);
(3) Pediatric Cardiopulmonary Assist System (pCAS) - a compact integrated pump oxygenator (Ension Inc.);
(4) *Infant Jarvik 2000 VAD* - an axial-flow
impeller pump, apically implanted pediatric VAD (Jarvik Heart, Inc)
(5) Pediatric VAD (PVAD) - designed as a pulsatile, pneumatic pump.

PumpKIN Clinical Trial
Janvier 2014

Infant Jarvik 2000 VAD : unique device à recevoir le financement pour continuer la recherche clinique

Début clinical trials prévus 2015 → STOP car INACCEPTABLE HEMOLYSE aux tests « in vitro »

Closing in on the PumpKIN Trial of the Jarvik 2015 Ventricular Assist Device

CrossMark

J. Timothy Baldwin,[a] Iki Adachi,[b,c] John Teal,[d] Christopher A. Almond,[e] Robert D. Jaquiss,[f] M. Patricia Massicotte,[g] Kurt Dasse,[h] Flora S. Siami,[i] Victor Zak,[i] Jonathan R. Kaltman,[a] William T. Mahle,[j] and Robert Jarvik[d]

PEDIATRIC CARDIAC SURGERY ANNUAL • 2017

PumpKIN Clinical Trial

Closing in on the PumpKIN Trial of the Jarvik 2015 Ventricular Assist Device

J. Timothy Baldwin,[a] Iki Adachi,[b,c] John Teal,[d] Christopher A. Almond,[e] Robert D. Jaquiss,[f] M. Patricia Massicotte,[g] Kurt Dasse,[h] Flora S. Siami,[i] Victor Zak,[i] Jonathan R. Kaltman,[a] William T. Mahle,[j] and Robert Jarvik[d]

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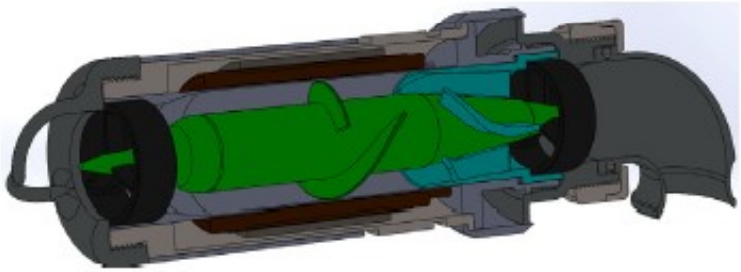


Figure 2 The Jarvik 2015 impeller blades (green) are attached to the rotor (also green). The stator blades (blue), the housing (gray), and cone bearing rings with posts (black) are stationary and only the rotor with the attached impeller blades move. The inflow is to the left, with flow from left to right in the illustration.

The developmental pathway for the Jarvik 2015 has been unique in that the government has taken a lead role and, as a result, it has involved the special productive collaboration and group effort of individuals from the VAD industry, various medical, engineering, and science academic departments and companies, and small business. Through their efforts to develop the device, specifically overcome the hemolysis issue, and plan the clinical study, the Jarvik 2015 is now well-positioned for another IDE submission to the FDA to begin the clinical trial in the near future. This trial, the PumpKIN clinical trial of the Jarvik 2015 VAD, is discussed below.

PumpKIN Clinical Trial

Vitro analyses tests (Texas Heart Institute) → minor modifications to the Infant Jarvik 2000 ↓ hémolysis 1) adding a radius to the impeller tips 2) the impeller speed was kept below 20,000 rpms.
No heating or cavitation.

Running the Infant Jarvik 2000 at 20,000 rpm limit the flow to <0.7 LPM → alternative ↑ diameter pump → lower speeds → flow range appropriate for pediatrics.

Many impeller blade designs ,evaluated using continuous flow devices, for in vitro hemolysis testing. Max level of NIH is 0.10 g/100L initial goal to achieve. Only 1 met the initial NIH goal over the specified pump speed/flow range → Protype selected as the next version Infant Jarvik VAD

Work completed 2015 + new outer hub diameter of the device was 15mm, new version named the "Infant Jarvik 2015 VAD" → "Jarvik 2015 VAD."

PumpKIN Clinical Trial

Pump 2 circular-arc impeller blades, a set of stator blades, 2 ceramic cone bearings

No inflow cannula, has an 8 mm outflow cannula, and a Jarvik Heart analogue controller

Jarvik 2015 larger than Jarvik 2000 VAD → ↑ rotor hub diameter
Outer diameter 15 mm Overall length 55 mm (AA battery)

Operating speed range 10,000 to 18,000 rpms, → flow range of 0.5 to 3.0 LPM at DP 45 mmHg

Design improvements (Surgeons)

1) an elbow on the outflow of the VAD to reduce the potential for kinking of the outflow graft since the flow must be redirected 180° due to placement of the pump and graft anastomosed to Ao

2) 8mm ePTFE outflow graft replaced with an 8mm gelatin-sealed, spiral- supported polyester graft by Vascutek → potential issues related to bleeding (due to needle punctures during suturing) + plasma weeping through the ePTFE grafts

3) Sub-diaphragmatic pocket < 8 kgs (Dividing left hemidiaphragm) (CT and MRIs study)

Changes from a parabolic blade arc to a circular one and the Increase in stator blades from three to four.

PumpKIN Trial

Feature	Infant Jarvik 2000 VAD	Jarvik 2015 VAD
		
Rotor Hub Outer Diameter	3.6 mm	5.6 mm
Flowpath Inner Diameter	6.1 mm	8.9 mm
Overall Length	47 mm	55 mm
Housing Outer Diameter	11 mm	15 mm
Rotor Length	37 mm	45 mm
Outflow Direction	0°	90°
Bearing Width	2.5 mm	3.2 mm
Number of Stator Blades	3	4
Number of Impeller Blades	2	2
Blade Shape	Parabolic-arc	Circular-arc
Radiused Impeller Blades	No	Yes
Speed Range	18,000 to 28,000 rpm	~10,000 to 18,000 rpm
Flow range	~.5 to 1.5 LPM	~0.5 to 3.0 LPM
Graft	8 mm ePTFE	8 mm gelatin-sealed polyester

PumpKIN Trial

NIH U.S. National Library of Medicine

ClinicalTrials.gov

Home > Search Results > Study Record Detail

Pumps for Kids, Infants, and Neonates (PumpKIN)

First Submitted Date ICMJE	October 31, 2016
First Posted Date ICMJE	November 3, 2016
Last Update Posted Date	February 26, 2020
Actual Study Start Date ICMJE	October 22, 2018
Estimated Primary Completion Date	April 2021 (Final data collection date for primary outcome measure)
Current Primary Outcome Measures ICMJE (submitted: February 24, 2020)	• To assess the clinical feasibility of the investigational Jarvik 2015 VAD by evaluating survival in the absence of severe neurological impairment or death, or device failure up to the clinical endpoint [Time Frame: 30 days]

Descriptive Information	
Brief Title ICMJE	Pumps for Kids, Infants, and Neonates
Official Title ICMJE	Pumps for Kids, Infants, and Neonates
Brief Summary	PumpKIN is a multicenter, two prospective, single-arm feasibility studies; One with Standard Cardiac Anatomy and one with Challenging Cardiac Anatomy evaluating the investigational Jarvik 2015 VAD in pediatric patients with heart failure. This feasibility trial will enroll 10 subjects, 5 Standard Cardiac Anatomy subjects reaching endpoints, and 5 Challenging Cardiac Anatomy subjects reaching endpoints at up to 7 sites in the US. The primary objectives of this investigational device exemption (IDE) clinical investigation are to assess the feasibility of using the Jarvik 2015 in pediatric patients with severe heart failure who require mechanical circulatory support. Feasibility will be assessed by evaluating the safety profile of the Jarvik 2015 device in eligible subjects.

PumpKIN Trial

Is the New Infant Jarvik 2015 Suitable for Patients<8 kg? In Vitro Study Using a Hybrid Simulator

Di Molfetta et al. Artif Organs 2019

Because of the difficulties to test a VAD in small animals, the FDA approved the use of the Infant Jarvik 2015 in children higher than 8 kg only (1). Therefore the aim of this work is to study the feasibility and reliability of the use of the Infant Jarvik 2015 in lower weight patients (<8 kg) using a hybrid model of the human cardiovascular system.

In this specific application, we verified that in the hybrid simulator the Infant Jarvik 2015 could be suitable for implantation in patient weighing less than 8 kg because of the stability of the device in respect to the cardio-circulatory changes in terms of suction and backflow phenomenon and because of the capability of the device in maintaining adequate patient hemodynamics.

PumpKIN Trial

First Human Implantation of A Miniaturized Axial Flow Ventricular Assist Device in a Child with End-Stage Heart Failure

Antonio Amodeo M.D. , Sergio Filippelli M.D. , Gianluigi Perri M.D. ,
Roberta Iacobelli M.D. , Rachele Adorisio M.D. ,
Francesca Iodice M.D. , Alessandra Rizza M.D. ,
M. Patricia Massicotte M.D., M.S. , J. Timothy Baldwin Ph.D. ,
Christopher S.D. Almond M.D., M.P.H.

Case Report J Heart Lung Transplant . 2019 Jul;38(7):789-793.

2018, 4 ans, 13 kgs 0.6 m2 de SC 3 runs ECMO/ST-VAD,
4 AVC/thrombosis sans consequences
Refuse greffe de la famille 3 semaines après implantation Plusieurs complications pendant Jarvik 2015
Thrombose pompe
Clopidogrel-Aspirine, Enoxaparine-HNF-Wafarin → Bivalirudine

PumpKIN Trial

TABLE. Lessons learned from the first implant of Jarvik 2015 LVAD in a 13-kilogram child with DCM.

Problem	Description	Lesson learned/observation
Pre-operative		
Pump fit in pericardial space is uncertain	Prior to pump placement, it is unclear how pump will sit within pericardial space, or whether creation of a diaphragmatic pocket would be preferable.	Pre-operative CT of chest facilitates fit assessment and surgical planning. No diaphragmatic pocket was required to place the pump, but no barriers to creating a pump pocket were identified by the surgical team.
Operative		
Ringed outflow graft is too stiff, and sutures holes tend to bleed	Stiff outflow graft is difficult to manipulate. Suturing the outflow graft directly to the aorta created too much tension on the aorta, with risk of obstruction and bleeding	Anastomosing the outflow graft to a Dacron chimney graft created less tension on the aorta and led to less bleeding. Also, allowing outflow graft to cross below the RV and curve up the right side of the mediastinum reduced the risk of graft damage on reopening the chest at transplant. The problem of the stiff outflow graft can also be alleviated by pealing back the radial graft support.
Prior ventriculostomy site from the EXCOR inflow cannula	Large ventriculostomy site from prior placement of the 9 mm EXCOR cannula complicated surgical placement of the Jarvik	Prior EXCOR cannula site can be used (with using the coring needle) allowing pump placement to be aligned (parallel) to the septum
Lack of a flow sensor	To keep the device small, no flow meter exists (similar to the adult Jarvik device).	Pump flow is estimated from the HQ curve (Figure 1B). Recommend posting the HQ curve at the bedside for quick reference. An LA line may be helpful for precise estimation of the pressure change across the device. However, the CVP is a useful surrogate if RV dysfunction is minimal, or well-compensated (low RAP) with medical support.
Post-operative		
The driveline cable is too short	Inadequate cable length to loop the cable in the abdomen to relieve stress in the event the driveline was pulled accidentally	Recommendation to Jarvik, Inc to increase the driveline cable length from its current size (21 cm) to the adult standard (30.5 cm) (recommendation approved by FDA and executed).
Driveline cable is too flexible which could injury the wires causing a fault	Driveline cable is too flexible at the point where the velour terminates, creating a potential fault point related to bend injury.	Recommendation to add a bend-relief device to the driveline to prevent wear on the driveline cable (recommendation approved by FDA and executed).
The power meter is calibrated up to 6 watts only, rather than 11 watts like the adult Jarvik.	Because the power meter is not calibrated beyond 6 watts, it is difficult to know how close the pump is to 11 watts, where the automatic pump stoppage (to avoid overheating) is trigged.	Increase the calibration range of the power meter from 2 to 6 to 1 to 11 (recommendation approved by FDA and executed)
Risk of pump thrombus	Despite axial-flow design, the miniaturized pump is still prone to thrombus	Key strategies to avoid pump thrombus: (1) ***early surgical hemostasis is critical*** to initiate antithrombotic therapy in a timely fashion; (2) bivalirudin appears to provide better protection than heparin (now approved by FDA as the primary anticoagulant for PumpKIN Trial); (3) interruptions to anticoagulation should be avoided; (4) conversion to conventional anticoagulants like warfarin or enoxaparin should be done cautiously, and higher target goals and higher doses of antiplatelet therapy may be needed in smaller subjects (e.g. <10 kg); (5) hypertension must be controlled meticulously because of the risk of lower flows, or even reversal of flow, that can precipitate pump or outflow graft thrombus. Blood pressure guidelines from the Advanced Cardiac Therapies Improving Outcomes Network (*Action*) may be useful BP targets to follow.
Risk of hemolysis	Because of its smaller size, some degree of hemolysis may occur more frequently with the Jarvik pump	Low grade hemolysis may be more common with the Jarvik pump. Lowering the RPM may be helpful provided pump flows are adequate at a given blood pressure. If transfusion is required, avoid older (>2 weeks) packed red blood cells which tend to be more fragile and susceptible to lysis with sheer stress.

Amodeo A et al. JHLT. 2019

PumpKIN Trial

Adachi I, Spinner JA, Tunuguntla HP, Elias BA, Heinle JS. ***The miniaturized pediatric continuous- flow device: A successful bridge to heart transplant.*** J Heart Lung Transplant. 2019 Jul;38(7):789-793.

….Two-arm prospective randomized study…randomly ….the Berlin EXCOR or the Jarvik Infant 2015 device, each group…44 patients… This trial may open the era of the use of implantable continuous-flow VADs in small children.

Short-term continuous-flow devices

Supporting pediatric patients with short-term continuous-flow devices

Jennifer Conway, MD,[a] Mohammed Al-Aklabi, MD,[b] Don Granoski, RRT,[c,d] Sunjidatul Islam, MSc,[a] Lyndsey Ryerson, MD,[c] Vijay Anand, MD,[c] Gonzalo Guerra, MD,[c] Andrew S. Mackie, MD,[a] Ivan Rebeyka, MD,[b] and Holger Buchholz, MD[b]

The Journal of Heart and Lung Transplantation, Vol 35, No 5, May 2016

From the [a]Division of Cardiology, Division of Pediatric Cardiology, University of Alberta, Edmonton, Alberta, Canada; [b]Division of Pediatric Cardiac Surgery, Stollery Children's Hospital, Edmonton, Alberta, Canada; Divisions of [c]Division of Pediatric Critical Care, Cardiac Surgery; and the [d]Stollery Children's Hospital, Pediatric Cardiac Critical Care, University of Alberta, Edmonton, Alberta, Canada.

- Thoratec Centrimag / Pedimag - Maquet RotaFlow, canules CEC / Berlin Heart
- 2005-2014, rétrospective, single center (Edmonton), 27 pts, 33 runs, 1 run= 1 event
- Primary outcome : decanulation (Greffe, recovery, long-term VAD, death)
- Complications : saignement (reprise pour hémorragie / hematome), neuro (AVC), infections (Germe isolé), ischémie d'organes (G-i, rate, foie, etc), device malfunction (Pièce/device à changer pour causes techniques autre de la thrombose)
- Statistique descriptive
- Gestione du malade : previous ECMO (Type, timing), CRRT, ajoute oxygenateur, anticoagulation (Timing start, cible anti-Xa, drains)

Table 1 Demographic and Clinical Characteristics of Patients With Short-Term Continuous-Flow Ventricular Assist Device Implant Based on Implantation Strategy

		Site of implantation of VAD		
Variables[a]	All patients	Left and systemic ventricle	Right ventricle	Biventricle
Patients	27	15 (56)	5 (19)	7 (26)
Total STCF-VAD runs	33	18	8	7
Age at implant, years	1.7 (0.1, 4.1)	0.7 (0.1, 3.6)	1.4 (0.2, 10.8)	3.5 (0.6, 16.5)
Weight at implant, kg	8.9 (3.7, 18.0)	7.2 (3.6, 14.8)	10.9 (3.8, 29.5)	14 (8.4, 41.0)
Female sex	15 (56)	9 (60)	2 (40)	4 (57)
VAD implantations, No.				
1	23 (85)	13 (86)	4 (66)	6 (100)
2	2 (7)	1 (7)	1 (17)	
3	2 (7)	1 (7)	1 (17)	-
Duration of support per run, days	12 (6, 23)	11.5 (7, 37)	12.5 (2, 28)	12 (9, 22)
Diagnosis at implantation	33			
Cardiomyopathy/myocarditis	11 (33)	5 (28)	3 (43)	3 (38)
Congenital heart disease[b]	14 (42)	10 (56)	2 (29)	2 (25)
Post-transplantation	6 (18)	2 (11)	1 (14)	3 (38)
Other	2 (6)	1 (6)	1 (14)	
Pre-implant ECMO	15 (45)	8 (44)	2 (25)	5 (71)
Oxygenator added to the circuit	20 (61)	9 (50)	5 (63)	6 (86)
Renal replacement therapy	21 (64)	11 (61)	4 (50)	6 (86)

ECMO, extracorporeal membrane oxygenator; STCF, short-term continuous-flow; VAD, ventricular assist device.

[a]Continuous data are presented as the median and interquartile range (25th quartile, 75th quartile) and categoric data as number (%).

[b]Congenital heart lesions (13 patients/14 runs): transposition of great arteries ($n = 3$), anomalous left coronary artery from the pulmonary artery ($n = 2$), Ebstein anomaly ($n = 2$), Shone complex ($n = 1$), bicuspid valve ($n = 1$), biventricular outflow tract obstruction ($n = 1$), Fontan ($n = 2$), and right atrial isomerism with unbalanced atrioventricular septal defect ($n = 1$).

Conway et al. STCF-VAD Support in Pediatric Patients
The Journal of Heart and Lung Transplantation, Vol 35, No 5, May 2016

Short-term continuous-flow devices

Table 2 Number of Runs and Duration of Support by Type of Device

Type of device	Runs (N = 33) No. (%)	Duration of support: Median (IQR) days	Duration of support: Min–Max days
CentriMag/PediMag	19 (58)	11 (6, 33)	2–75
RotaFlow	8 (24)	9 (3, 19.5)	1–37
CentriMag/PediMag and RotaFlow	6 (18)	20 (12, 33)	9–70

IQR, interquartile range (25th, 75th quartile).

Bien dépassée la limite de 14 jours (définition short-term device)

Conway et al. STCF-VAD Support in Pediatric Patients
The Journal of Heart and Lung Transplantation, Vol 35, No 5, May 2016

Short-term continuous-flow devices

Table 3 Cause of Death During Hospital Admission for Short-Term Continuous-Flow Ventricular Assist Device Run

Patient	Diagnosis	Duration of ST-CF VAD support (days)	Death on device[a]	Cause of death	Comments
1	HTx and RV failure	75 days pre-HTx; 6 days post-HTx	Yes	MOD post-HTx	CentriMag pre-HTx for myocarditis and post-HTx for RV failure
2	Allograft vasculopathy	37	No	Ischemic bowel	Converted to ECMO for sepsis before death
3	Primary HTx and BiV failure	6	No	MOD post-second HTx	On ST-CF VAD till re-HTx, died after 2nd HTx after support withdrawn
4	RAI, AVSD PS and BiV dysfunction	68	Yes	Heart failure	One-way wean due to MOD
5	Post-Fontan operation	2 runs: 10 days and 45 days	Yes	MOD	Native heart excised due to intramyocardial hematoma
6	Transposition of the great arteries	7	Yes	Renal failure, with severe uncontrollable fluid overload	Therapy withdrawn
7	BiV outflow tract obstruction with LV dysfunction	4	No	Died post-HTx from MOD	Was converted to ECMO pre-HTx and received HTx from ECMO
8	Bicuspid aortic valve and endocarditis	22	Yes	MOD	
9	Neonatal Ebstein anomaly	2	No	Sepsis with MOD	Converted to ECMO before death

AVSD, atrioventricular septal defect; BiV, biventricular; ECMO, extracorporeal membrane oxygenation; HTx, heart transplant; MOD, multiorgan dysfunction; PS, pulmonary stenosis; RAI, right atrial isomerism; RV, right ventricle; ST-CF, short-term continuous-flow; VAD, ventricular assist device.
[a]Death on device or within 1 month of weaning.

Conway et al. STCF-VAD Support in Pediatric Patients
The Journal of Heart and Lung Transplantation, Vol 35, No 5, May 2016

Short-term continuous-flow devices

- TIME FOR DECISIONS - TIME FOR MYOCARDIAL RECOVERY - DETAILED END-ORGAN ASSESSEMENT
- STCF-VAD vs ECMO (MORTALITE')
- SORTIE HOPITAL 67% (United Network Organ Sharing 72%, médian durée 11 jours)
- Patients HAUT-RISQUE (ECMO avant/pendant, CRRT)
- Circuits/pompes SHORT-TERM mais usage PROLONGE'

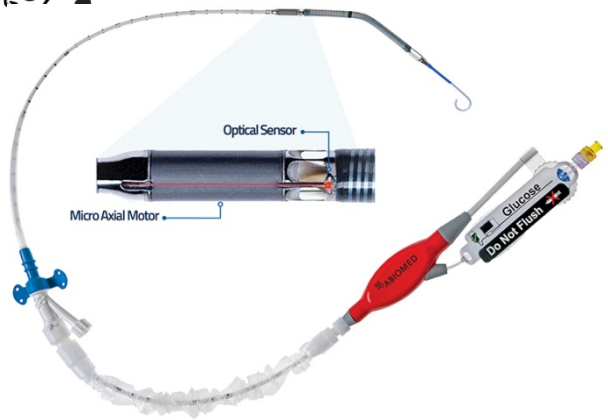
❑ changer le circuit-pompe 4-6/semaines (Haj-Yahia et al, 4 adultes)

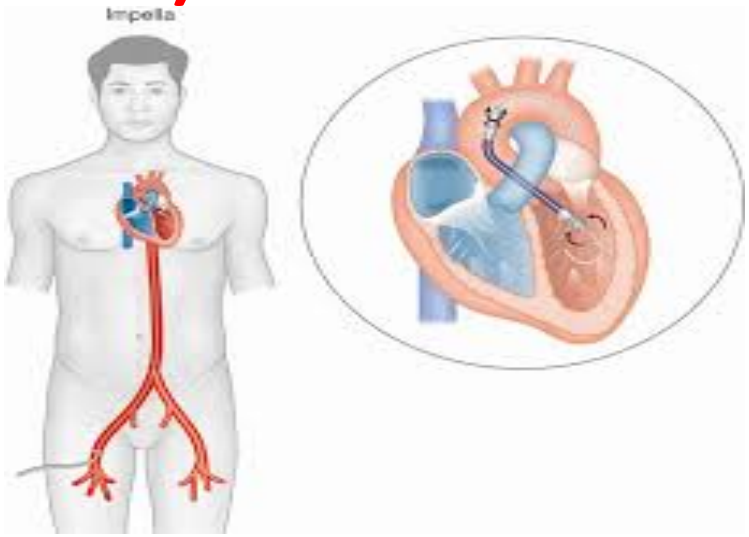
❑ Edmonton surveiller, changer pièces circuits si hemolyse/thrombose

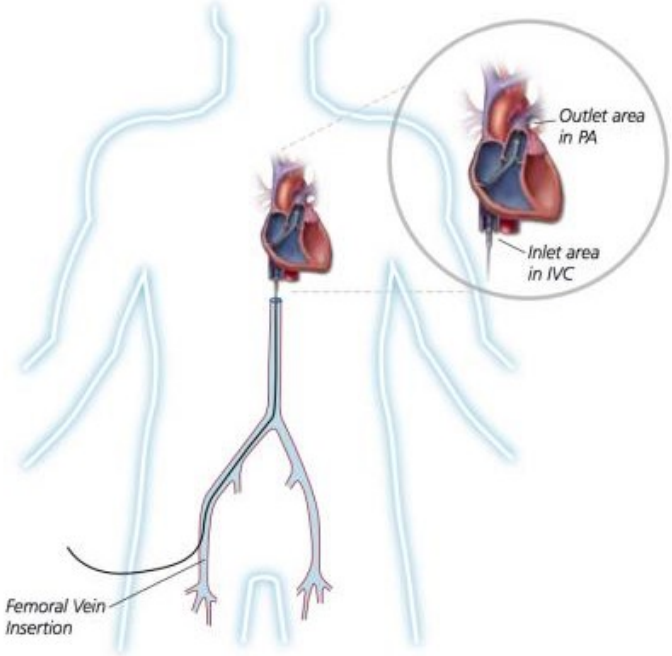
- RVAD : pas risque AVC ischémique ; dysfonction VD in greffe, L-VAD, SDRA ; Ebstein
- < COMPLICATIONS VS ECMO - VAD LONG DUREE
- TIMING, STRATEGIE ANTICOAGULATION

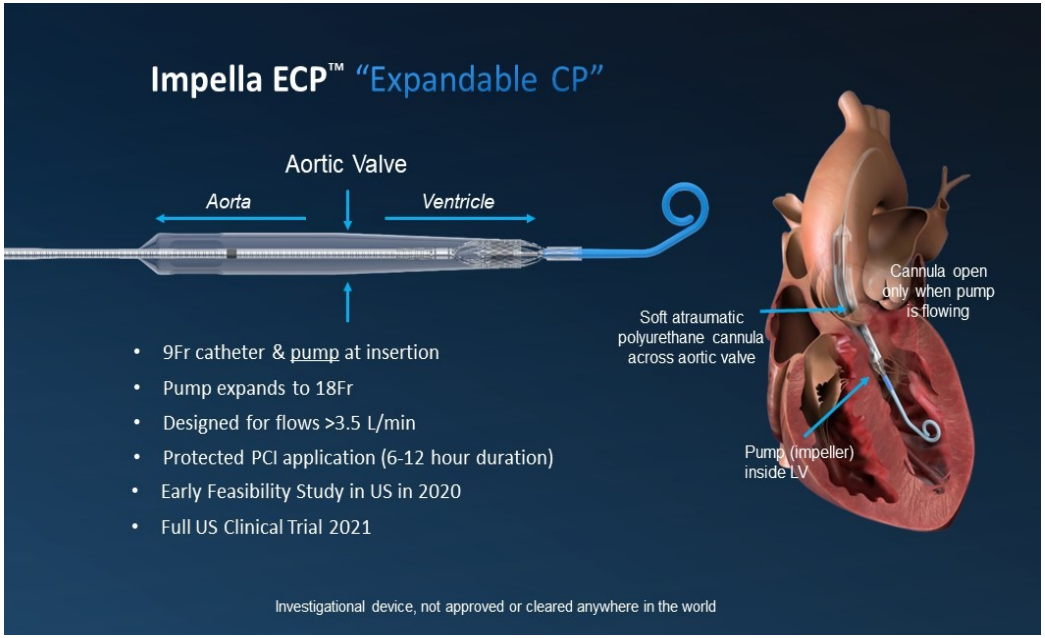
Conway et al. STCF-VAD Support in Pediatric Patients
The Journal of Heart and Lung Transplantation, Vol 35, No 5, May 2016

Impella (L and R) in Pediatric









Short-term continuous-flow devices

ASAIO Journal 2017

Case Reports

First Report of Biventricular Percutaneous Impella Ventricular Assist Device Use in Pediatric Patients

JAVIER J. LASA,*† DANIEL A. CASTELLANOS,† SUSAN W. DENFIELD,† WILLIAM J. DREYER,† SEBASTIAN C. TUME,* HENRI JUSTINO,† AND ATHAR M. QURESHI†

Percutaneous Impella RP use for refractory right heart failure in adolescents and young adults—A multicenter U.S. experience

Catheter Cardiovasc Interv. 2020;1–6.

Athar M. Qureshi MD[1] | Mariel E. Turner MD[2] | William O'Neill MD[3] | Susan W. Denfield MD[1] | Nima Aghili MD[4] | Amit Badiye MD[5] | Radhakrishan Gandhi MD[6] | Behnam Tehrani MD[7] | George Chang MD[8] | Jared K. Oyama MD[9] | Shashank Sinha MD[7] | Nicolas Brozzi MD[5] | Brian Morray MD[10]

MCS in CHD

Single Ventricular Assist Device Support for the Failing Bidirectional Glenn Patient

(Ann Thorac Surg 2020;110:1659-66)

Katsuhide Maeda, MD, Teimour Nasirov, MD, Vamsi Yarlagadda, MD, Seth A. Hollander, MD, Manchula Navaratnam, MD, David N. Rosenthal, MD, John C. Dykes, MD, Beth D. Kaufman, MD, Chris S. Almond, MD, Olaf Reinhartz, MD, Jenna Murray, NP, and Sharon Chen, MD

Department of Cardiothoracic Surgery, Stanford University, Palo Alto, California; Department of Pediatrics, Stanford University, Palo Alto, California; and Division of Department of Anesthesiology, Stanford University, Palo Alto, California

- **Retrospective review describes an institutional experience with VAD support for patients with BDG from April 2011 to January 2019**
- **A total of 7 patients with BDG (weights, 5.6 to 28.8 kg; ages, 7 months to 11 years) underwent VAD implantation.**
- **3 patients underwent implantation of Berlin Heart EXCOR, 2 had HeartWare HVADs and 2 patients underwent implantation of paracorporeal continuous flow devices**
- **2 alive et 5 death**

- The surgical strategy and postoperative management of VAD with BDG are still evolving

- Successful support can be achieved with:
  (1) both pulsatile and continuous flow pumps
  (2) atrial or ventricular cannulation
  (3) with or without BDG take-down

- Surgical strategy should be determined by individual patient anatomy, physiology, and condition

- OUTCOME ?????

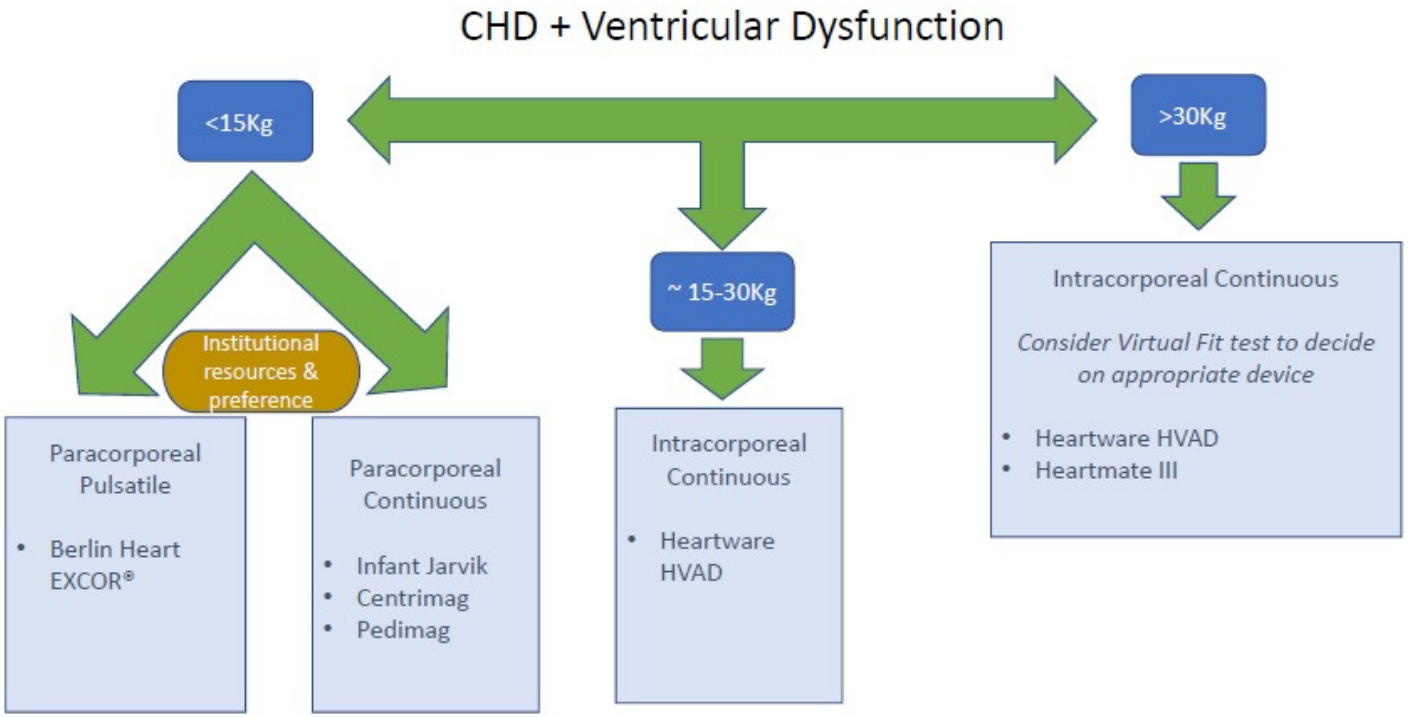
Maeda Ann Thor Surgery 2020

MCS in CHD

Mechanical circulatory support in pediatric and adult congenital heart disease

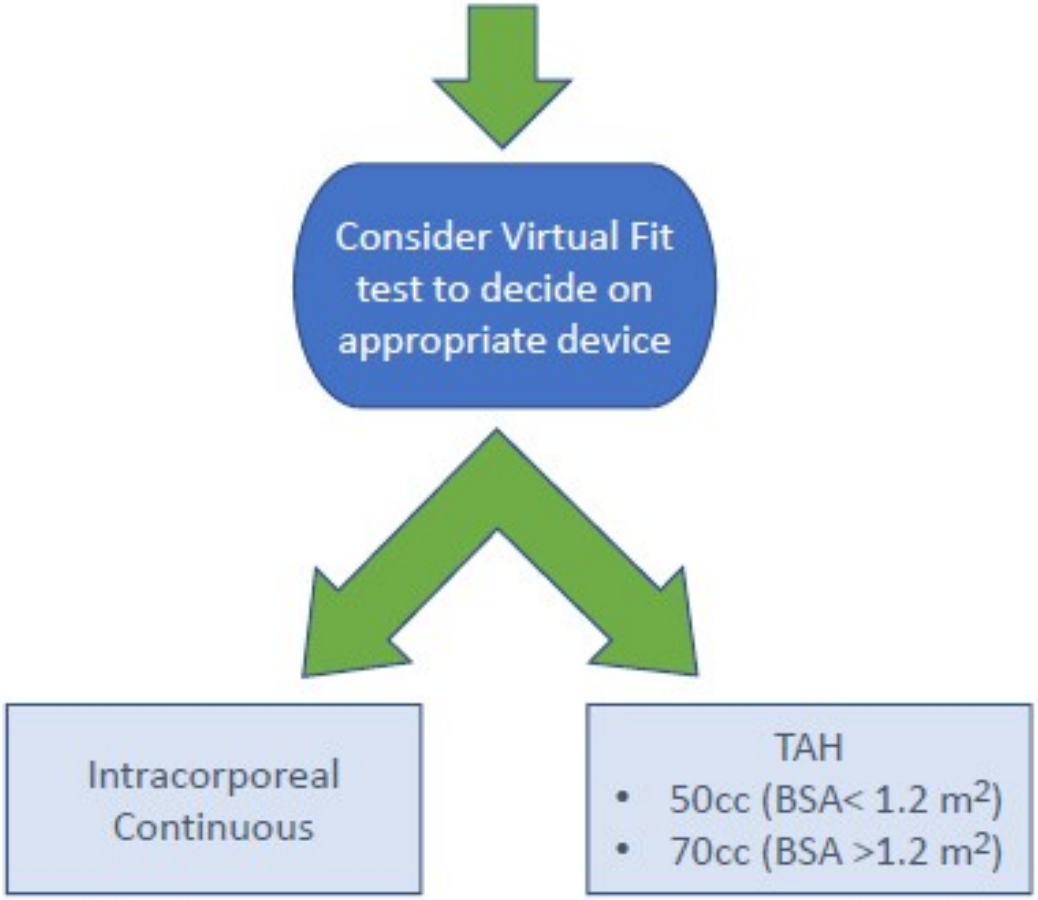
Ramiro Lizano Santamaria, MD, Aamir Jeewa, MD, Ari Cedars, MD, Holger Buchholz, MD, Jennifer Conway, MD

Canadian Journal of Cardiology October 2019



MCS in CHD

Failing Fontan Physiology
with ventricular dysfunction*



Santamaria Can J Cardio 2019

MCS in ACHD

Transplant and mechanical circulatory support in patients with adult congenital heart disease

James Monaco[1], Amber Khanna[1], Prateeti Khazanie[1] *Heart Fail Rev.* 2020 July ; 25(4): 671–683.

- **All aspects of GUCH in advanced HF about Transplantation and MCS**

- **Continued improvement in MCS utilization to improve waitlist outcomes for GUCH**

- **Mechanical support of the systemic right ventricle with a subpulmonic left ventricle and MCS in Fontan population**

- **Mechanical circulatory support in ACHD more robust outcomes data become available to support its benefit → Durable VADs increasingly popular option both for optimizing patients listed for transplant or possible destination therapy**

- **Outcomes in ACHD MCS are likely to improve as perioperative experience increases and as patient selection trends toward less critically ill patients**

MCS in CHD

Considerations for Advanced Heart Failure Consultation in Fontan Patients:

Guidance for primary cardiologists

action
ADVANCED CARDIAC THERAPIES IMPROVING OUTCOMES NETWORK

HARMONIZED PROTOCOL

BACKGROUND

To aid in decision-making on timing of referral of Fontan patients for advanced heart failure consultation with the aim of improving timely referral and facilitating collaborative care to enhance patient outcomes.

Patient population: Fontan patients

Considerations for referral by type of clinical Fontan dysfunction

(recognizing overlap exists between categories)

Cardiac/Systemic Ventricular Dysfunction

1) Severe[1] systolic dysfunction by echocardiogram, MRI, or cardiac catheterization.
2) Moderately depressed (by qualitative assessment) systolic function on imaging when accompanied by ≥moderate systemic AV valve regurgitation.
3) Significant growth derangement or failure to thrive including cachexia or linear growth failure
4) Decreasing exercise tolerance by patient report or as measured on sequential formal exercise testing or 6-minute walk
5) Significant electrophysiologic abnormalities, including recurrent arrhythmias despite therapy, implantation of a cardiac pacemaker, or aborted sudden cardiac death event

Fontan Pathway Dysfunction

1) Symptomatic, chronic fluid overload persisting despite new or increasing diuretic therapy
2) Occurrence of chronic pleural effusions or ascites, chylous or nonchylous, refractory to therapy and occurring outside the initial Fontan post-operative period
3) Major hemodynamic disturbance *resulting in symptoms* despite therapy including: low systemic cardiac output, diastolic ventricular failure, significantly elevated Fontan pressure, or symptomatic cyanosis

Lymphatic Dysfunction

1) Protein-losing enteropathy that has failed medical therapy and requires multiple hospital admissions in a 12-month period or PLE requiring repeated albumin infusions to treat symptoms despite standard PLE medical therapy
2) Plastic bronchitis requiring chronic therapy

Extra-cardiac Dysfunction

1) Hemoptysis requiring evaluation that is unrelated to an infection and persists after standard intervention
2) Liver disease with impaired synthetic function/abnormal liver function testing or undergoing evaluation for liver transplantation
3) Chronic kidney disease – Stage 3 or greater[2]

Destination-Therapy Ventricular Assist Device in Children: "The Future Is Now"

Canadian Journal of Cardiology
Volume ■ 2019

Hari Tunuguntla, MD,[a] Jennifer Conway, MD,[b] Chet Villa, MD,[c] Adam Rapoport, MD,[d] and Aamir Jeewa, MD[d]

- **INTREPID (Investigation of NoneTransplant-Eligible Patients Who Are Inotrope Dependent), REMATCH (Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure)**
- **Evénements Indésirables VAD différences Adulte vs Pédiatrique**
- **Sélection patients**
- **Type de VAD**
- **DT VAD Dystrophie Musculaire (Amodeo, Rome)**
- **DT VAD Failing Fontan (plusieurs type de VAD ; chirurgie)**
- **Améliorer QOL plus que survie**

Quality of Life

The Ventricular Assist Device in the Life of the Child: A Phenomenological Pediatric Study

Michael A. van Manen

Qualitative Health Research
2017, Vol. 27(6) 792–804

Without a doubt, there are significant emotional and psychosocial burdens of living with a VAD. Caregivers need to support children whether it means making sense of the life situation, dealing with the worries of medical complication, or simply living with the sensations of the mechanicity of the device. Just like in other medical contexts, we need to consider how children can habituate to the VAD so they can focus on the ordinary and routine aspects of their lives even in the context of dependency and uncertainty (Stewart, 2003). Recognizing the VAD may also

Quality of Life

ORIGINAL ARTICLE

Pediatric Transplantation. 2019;

Parental responsibility for pediatric ventricular assist devices: Views of families on the acceptability of hospital discharge

Lisa Crowe[1] | Emma Simpson[2] | Zdenka Reinhardt[2] | Judith Rankin[1]

- Teams efforts to provide each family with private time alone, if at all possible
- Mobile paracorporeal technology is expected to improve the freedom /quality of life, but discharge home not expected until proven safety and benefit
- Families struggle with the emotional and practical challenges of the bridging period and experiences of helpful interventions need to be shared between hospital teams
- In this single-center study, families showed a lack of understanding for the complexities of transplant listing status and criteria in general, with a tendency to oversimplification
- Transplant teams should ensure that a change in listing status does not become a barrier to discharge home, if this is desired and felt to benefit the child
- Goal setting and discharge planning should deal with the specific concerns of families and should be individualized and achievable
- Development of a discharge program, co-designed with all relevant parties. Working with families around discharge will ensure their views and concerns

Conclusions

- Network (Pedimacs, Paedi-EUROMACS, ACTION)
- Education
- Indication
- CHD
- Role des assistances temporaires hors ECMO
- Teamwork
- Centralisation
- Sélection patients
- Complications
- QOL

Questions ?