UNIVERSITA' DEGLI STUDI DI PADOVA

Corso di Laurea Magistrale in Medicina e Chirurgia

Presidente: Prof.ssa Maria Luigia Randi

TESI DI LAUREA:

Intracorporeal ventricular assist device implantation in pediatric patients and preoperative patient-tailored imaging to assess feasibility

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INDICE

1 Introduction

Although heart transplant remains the best standard and definitive therapy for end-stage cardiac failure in children (as in adults), there is still significant mortality while waiting for transplantation. Actually, there are two main options to use for mechanical assistance to circulation for pediatric patients who undergo severe heart failure, which can be caused for example by cardiomyopathies, myocarditis, or progressive loss of ventricular function after palliation surgery for congenital heart diseases; in which failure of the medical therapy makes necessary for the child a temporary mechanical cardiocirculatory support.

The first possibility is to use extracorporeal membrane oxygenation (ECMO).The use of this practice for children started in the late 1960s, but the real increase in the use of this technique was in the 2000s. ECMO has indeed high rates of severe complications, such as for example bleeding and coagulopathy, stroke, and infections, and the rate of such complications increases increasing the time the patient is supported; literature reports only 13% of survival for patients using ECMO for more than 28 days[1].

The other options for temporary circulation support are given by the ventricular assist devices (VADs), which have been initially approved for a really short-term use (6 hours) in acute cardiogenic shock after right heart failure, and then possibly extended to 30 days as a humanitarian use device. Actually, there are several types of temporary circulatory support devices, with different technologies. VADs can be mostly divided into two categories: pulsatile VADs, which resemble the natural pulsation of the heart, and continuous flow VADs (cfVADS), which use a motor to continuously draw blood to the systemic circulation producing a flat flow, without pulse pressure. Continuous flow VADs are usually smaller, intracorporeal, and more durable than pulsatile ones, which are bigger and paracorporeal, and they can use a centrifugal flow (e.g. HeartWare VAD) or axial pump (e.g HeartMate II LVAD), both with a central rotor and permanent magnets (magnetic levitation suspension, MagLev^{TM}). Furthermore, VADs can

support only the left ventricle (LVAD), only the right ventricle (RVAD), or both (BiVAD). An other important division we can make between different VADs is into VADS giving short term support, such as IABP ir Impella, and the ones giving long term support, This is important for the choice of the correct device accorting to the needs of the patient.

Pediatric-sized pneumatically driven VADs for infants and small children were introduced into the clinical routine in 1992. The development of miniaturized pump systems followed the first reported case of an 8 years old child with end-stage heart failure supported with an adult-size VAD (the first Berlin Heart) until later transplantation. [11]

So, some adult-sized VADs well supported larger children and teenagers to transplant. For smaller children waiting for heart transplant, a pneumatic pediatric-specific cfVAD, the EXCOR, was developed in Germany by Berlin Heart GmBH[9].The Berlin Heart device is designed to support one or both ventricles, it is available in sizes suitable for children of 3 kg to adult size. The EXCOR was implanted for the first time in the USA in 2000 but did not had widespread use until 2004. Before that, encouraging experiences have been reported, but these were only limited to small single centers. Both theese techniques can be used for bridge to recovery, bridge to decision, or bridge to transplant.

2 Extracorporeal membrane oxygenation (ECMO) support

Extracorporeal membrane oxygenation (ECMO) is a lifesaving procedure used for babies, children and adults with life-threatening cardiocirculatory and oxigenation issues, providing the time for the body to recover replacing temporary the work of the heart and lungs. It doesn't treat the undergoing pathology, buti t gives the time to heal. It can be considered a modified form of heart-lung bypass (CEC) but it can be used for a longer time (days to weeks) than the CEC machine used in the operating room during open-heart surgeries, but the principle and the functioning is very similar to CEC. The ECMO machinery is composed by:

- a centrifuge roller pump, replacing heart function
- a membrane oxigenator (artificial lung)
- a heat exchanger, to avoid heat loss in the circuit
- a gas blender (0_2/air) and gas lines
- the circuit (drain and reinfusion lines)
- the cannnulae, inserted in the large vessel of the patient, to draw and reinsert the blood

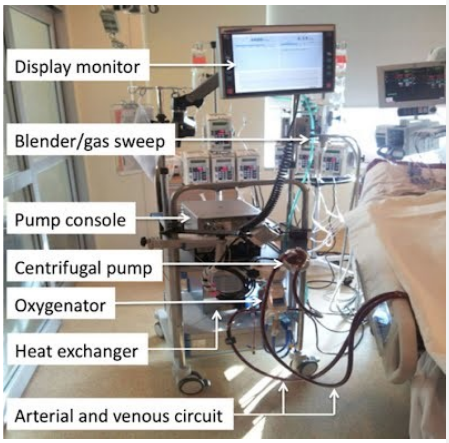


Figure 1 ECMO components

2.1 Functioning of ECMO machine

Blood is drawed from the patient trought a cannula placed surgically in a large venous blood vessel, thanks to the pump, it passes the membrane oxigenator and heat exchanger, and after being oxigenated is reinfused through the second cannula, which is venous (VV-ECMO) if only respiratory support is needed, or arterious if also cardiocirculatory support is needed (AV-ECMO). There are two different techniques for cannulation: in the central cannulation, similar to the one used in CEC, used if the patient underwent cardiothoracic surgery, the venous drainage is placed in the right atrium, and the arterious reinfusion cannula is in the ascending aorta, while in peripheral cannulation used if the patient had no surgery, the venous drainage is in the common femoral vein or right inner giugular vein, and the arterious cannula is in the common femoral artery or in the axillary artery. The patient is sedated and anticoagulated, usually with heparin, to avoid clotting, the surgeon inserts the cannulae in the chosen vessels and then an x-ray is performed to ensure the correct positioning of the cannulae, and the patient is connected to the circuit and monitored by the ECMO team for all the duration of the treatment. An other important difference with CEC is the absence of the cardiotome in ECMO.

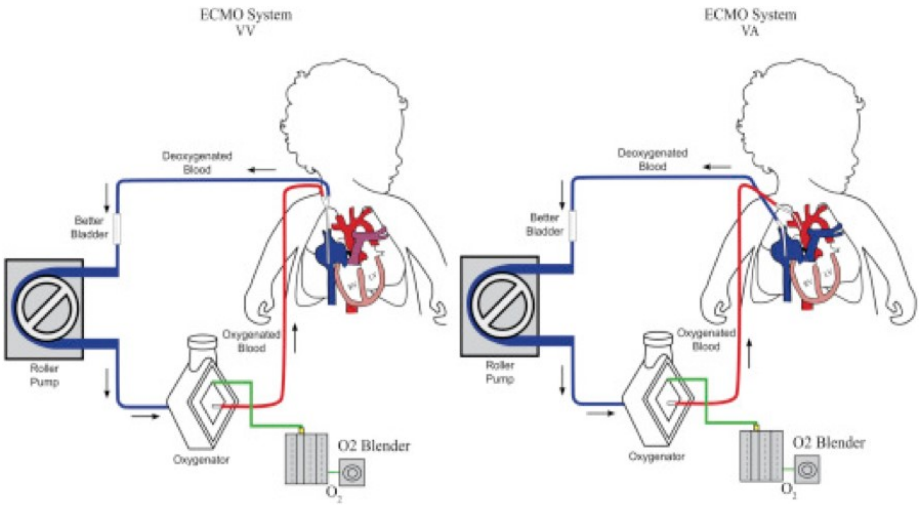


Figure 2 ECMO functioning scheme

But there are some important differences to keep in mind in using ECMO in pediatric patients compared to adults: for children there are different indications (reported in the next paragraph), different setup of the circuit and cannulae implantation sites. The Extracorporeal Life Support Organization (ELSO) is the largest database providing regular reports on international growth, outcomes, complications, and technology in ECMO practice. Traditionally there is an annual report focusing on adults and another one on pediatrics. The last ELSO report showed that 71% of ECMO implants were in children, and neonates were 47% of the whole cohort. [12] In the scheme below, the machinery and cannulation positioning points used for children are illustrated, for both AV and VV ECMO procedures.

2.2 Indications

Traditionally pediatric ECMO is indicated in congenital heart surgery (if weaning from CEC was not possible after the surgery, defined as post-cardiotomy ECMO). Then the indications have been extended to children with cardiogenic shock requiring inotropic support, and also for out-of-hospital cardiac arrest. In all of these cases, the cardiopulmonary support is given in the form of a veno-arterial ECMO. The other main indications for pediatric ECMO are resumed in the table below [12].

Table 1 indication to pediatric ECMO

Common indications for ECMO in pediatrics

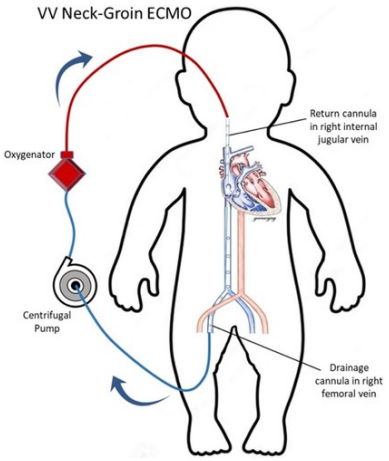
Indications	Neonate	Pediatric
Cardiac	Congenital defect: ❖ Hypoplastic left heart syndrome; ❖ Left ventricular outflow obstruction; ❖ Right ventricular outflow obstruction; ❖ Septal defects	Congenital defect: ❖ Left ventricular outflow obstruction; ❖ Right ventricular outflow obstruction; ❖ Septal defects
	Cardiomyopathy (bridge to recovery, transplant or long-term MCS)	Cardiomyopathy (bridge to recovery, transplant or long-term MCS)
	Myocarditis	Myocarditis
Respiratory	Meconium aspiration syndrome	Pneumonia (viral/bacterial/aspiration)
	Persistent pulmonary hypertension of newborn/persistent fetal circulation	Acute respiratory distress syndrome
	Respiratory distress syndrome	
	Congenital diaphragmatic hernia	
	Pneumonia (viral/bacterial/aspiration) Sepsis	

2.3 pediatric ECMO circuits and implantation techniques[10]

The pediatric population includes a wide range of weights and dimensions to deal with, so there is the need for different circuits and cannulas facing each category. For neonates and infants weighing until 15 kg the circuit contains about 250 mL of priming volume with flow ranges of about 1.7 L/min. For patients above 15 kg the priming solution volume is about 750 mL, with a flow rate up to 7.0 L/min, a flow which is sufficient also for adult patients.

Also cannulae implantation sites, as mentioned above, are different in children, for many reasons. In adults and emergency situations the femoral access is the most used. On the other side, in children before the walking age, femoral vessels are not sufficiently developed to face ECMO cannulation. In neonates, infants or small children the neck vessels or large central vessels (after median sternotomy) are preferred. The advantages of neck cannulation is that it's rapid to perform in emergency situations, such as CPR, also without interrupting chest compressions. Furthermore, using the ascending aorta or the right atrium as cannulation sites allows higher flow rates. Theorically neck cannulation may block the antegrade blood flow to the RCA, increasing the risk of stroke. However, there is no clear evidence in literature for this occurrence.

For pediatric VV ECMO implantations, traditional sites are the jugular vein and femoral vein (VV neck-groin ECMO). Implantation is ultrasound or X-ray guided, to guarantee the correct orientation of the cannulae. The proper position of the cannulae must be then confirmed with echocardiography.



3 The VADs

The VAD device selection is a critical issue for pediatric cardiocirculatory support, which is influenced as mentioned in the introduction, by several factors: patient size, type of support (LVAD or BiVAD), the duration of the period of support, the goal of support, and device availability, that for pediatric use is limited as well. The algorithm showed in the table below divides the device selection by time of support needs and aim of the treatment, guiding in the choice of the proper device. [18]

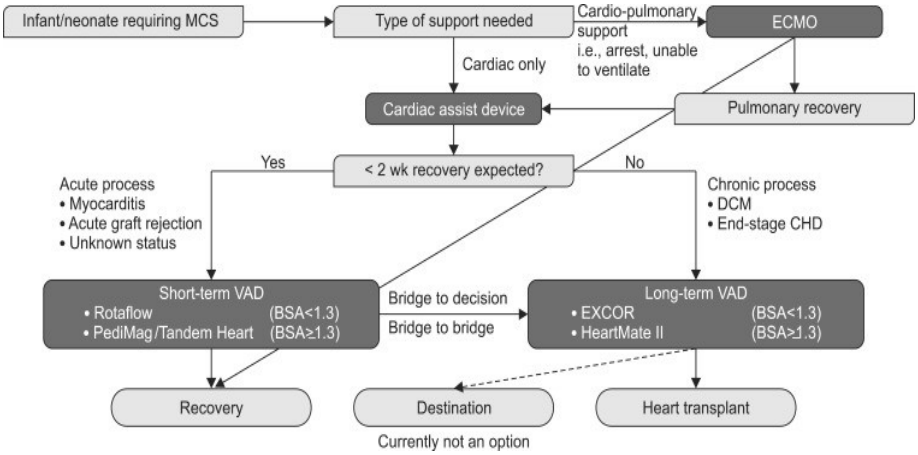


Table 2 algorythmfor the choice of the proper CMS device

The Berlin Heart EXCOR paracorporeal pulsatile VAD, showed in the next paragraph, gained FDA approval (december 2011) and is the only VAD approved specifically for pediatric use, even if, actually cfVADs have replaced pulsatile devices. [16] In fact, a significant incidence of adverse events such as embolic stroke, bleeding and infection incentivized some pediatric centers to use for children adapted adult implantable continuous-flow devices. The configuration of the circuit in short-term VAD support is very similar to ECMO. The great difference between the two systems is that in ECMO the oxygenator is incorporated, which can be source of inflammatory and coagulation problems related to ECMO.[17]

3.1 the EXCOR® Pediatric Berlin Heart

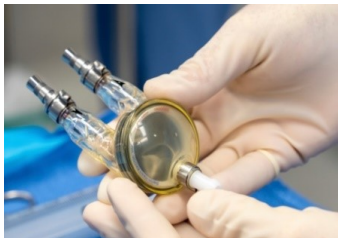


Figure 3 a Berlin Heart excor pediatric device

EXCOR® Pediatric is a external paracorporeal pulsatile VAD, which can be used as a bridge for short to long-term support of both left and right ventricular function (figures 3, 4 and 5). It is indicated by the producing company for children of all age groups with life-threatening heart failure after the failure of conservative therapeutic options. EXCOR® Pediatric is specifically designed for young patients, from newborns to teenagers. it is available with 10, 25, 30, 50 and 60 ml pump sizes, as well as the recently available 15 ml size pump (figure 4). In November 2019 a new mobile EXCOR System for children was introduced.

Figure 4 different sizes of EXCOR device

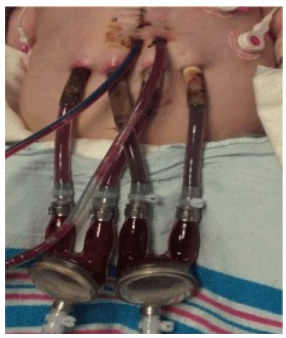


Figure 5 a biVAD EXCOR Berlin Heart

The same producing company has developed the same model also for adult patients. The EXCOR® is a pneumatic ventricular assist device: a triple-layer curved membrane separates the blood and air sides of the pump and it is set in motion through alternating pressures originating from a driving system and channeled into the pump via a tube. If positive pressure is applied the membrane ejects the blood of the blood chamber into circulation. Applying a negative suction pressure instead, the pump fills with blood. Valves in the inflow and outflow tracts ensure unidirectional circulation. The blood pumps differ in the size of the volume of blood displaced in each stroke, and the pump setting determines how often the membrane moves in a minute. That rate is chosen according to patient's requirements and conditions.[13] Actually literature reports several studies [9, 14,15] about this devices, showing a good outcame for them also after

months of use and a greater post-transplant overall survival compared to ECMO. It is considered a long-term VAD device. It is the most common device used as a BiVAD support, often with a smaller pump used as RVAD placed in the right ventricle, and a bigger sized pump in the left one (figure 5).

3.2 The pediMAG™ Thoratech centrifugal pump

The PediMag™ is a pediatric extracorporeal continuous flow device (cfVAD) based on a magnetically levitated centrifugal pump, similar to ECMO. The device can reach a flow of 1.5 L/min, and has been implanted in more than 650 pediatric patients worldwide and its use as a short- term temporary VAD is continuing to grow. The PediMag device is indicated for patients weighting less than 3 kg, it is applied through a central cannulation throught sternotomy, and may be used for transition to a long-term device. [18] The same company, Thoratech, produces the larger pump centriMAG, used in adults and larger children. It has been shown[6] that this kind of short term device can successfully bridge pediatric patients to recovery, to a long-term device, or to transplant, with an acceptable risk profile. These devices were initially designed for short-term support, but a longer support is possible and may be an alternative approach for patients not suitable for long-term devices.

Figure 6 a pedi MAG Thoratech device

3.3 Impella® Abiomed devices used in children

The Impella series is a family of percutaneously delivered ventricular assist devices (pVADs) composed by a coaxial micropump settled into a vascular catether, positioned through the aortic valve by retrograde femoral artery access. Its distal extremity, in the left ventricle, draws blood in the ascending bypassing the valve and reducing the left ventricle loading and giving a better hemodynamic. The inner device is then connected externally to a console, to a physiological solution sac and a purge fluid sac.

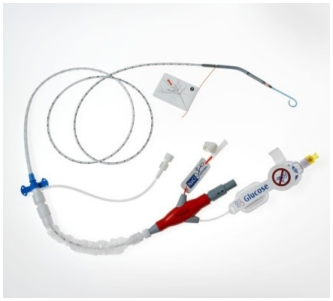


Figure 7 Impella 2.5

The Impella® 2.5 is the smallest heart pump of the Impella series. It works by drawing blood from the left ventricle out from the catheter into the ascending aorta, bypassing partially or totally the left ventricle. It can deliver about 2.5 L/min of flow, the implantation is performed through a standard catheterization procedure of the femoral artery to the ascending aorta, crossing the valve to reach the left ventricle. It has a 12 Fr micro-axial pump and 9 Fr Catheter.

Figure 8 Impella CP

The Impella CP™ operates on the same platform as the Impella 2.5, but it has an increased flow.

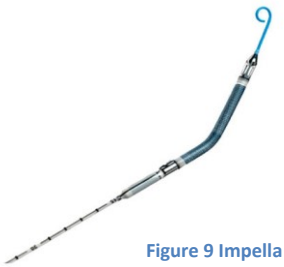


Figure 9 Impella 5.0

The Impella 5.0 model can carry up to 5.0 L/min of forward flow blood from the left ventricle to the aorta, and it's the smallest 5.0 L/min Heart Pump. It has a 9 Fr catheter and a 21 Fr micro axial pump. The Impella 5.0 can be implanted via femoral artery or the axillary artery. The femoral or axillary approach is determined primarily by the expected support duration and the aim of support. If the duration is >5 days with possible extubation and mobilization, the axillary approach may be preferred. [27]

The series include salso a right assistance device, the Impella RP® Catheter, that delivers blood from the inferior vena cava, through the cannula to the outlet in the pulmonary artery. This model can be implanted through the femoral vein, to the right atrium, across the tricuspid and pulmonic valves, to the pulmonary artery. The Impella RP® model is indicated for circulatory assistance up to 14 days in pediatric or adult patients with right heart failure.[26] The Impella CP and RP can be used also simultaneously to obtain a bi-ventricular support.

Figure 10 Impella RP

The use of these kind of devices in pediatric population, limited by their small size of vessels and cardiac chambers, was firstly indagated in animal models[19] or in sporadic case series,[20, 21] but then, several multicenter retrospective studies[22,23,24] have explored the use of the Impella family of catheters as mechanical circulatory support in children and adolescents with severe heart failures, initially only off-label, but showing acceptable profile risks for pediatric use, even if more data are necessary to define better the patient selection and improve the performance for this technique.

Furthermore, it has been proved that Impella microaxial-flow pump unloads left ventricle in cases of heart failure more effectively than ECMO[25], counting that an insufficient left ventricle unloading may not be advantageous for an efficient myocardial recovery. Impella devices are currently approved by FDA to provide short term circulatory support.

3.4 Intra aortic balloon pump (IABP)

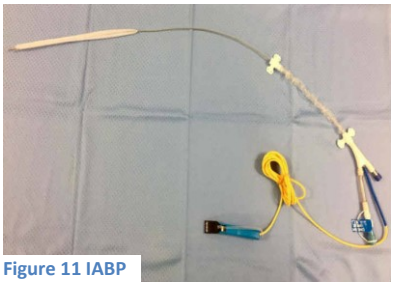


Figure 11 IABP

The IABP is a temporary circulatory support method widely used in adult patients, less in pediatric population. . Its use in pediatric population was firstly described in 1989,[28] but despite the availability of pediatric size balloons, ranging from 2.5 to 7 ml of gas volume mounted on small catethers (4 or 5 Fr) for infants and children up to 18 kg, and pediatric materials, its use in children was not so common.

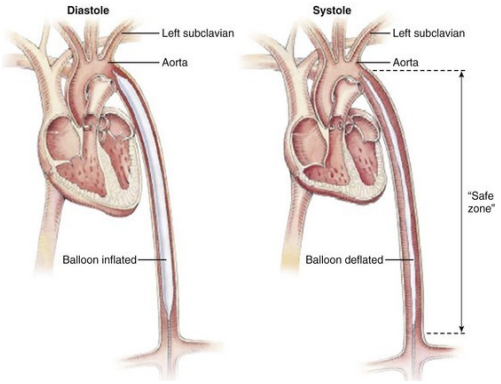


Figure 12 IABP functioning

The IABP is an expandable polyethylene balloon attached to the tip of a catheter and inserted via percutaneous x-ray guided femoral access into the descending aorta, distally to the origin of left subclavian artery. It can be considered ad an LVAD, giving support to the left ventricle. The correct positioning and timing of the balloon is extremely important to avoid complications, and it must be assessed by post procedure echocardiography.[34] The balloon is cyclically filled and emptied of helium supplied by a cylinder attached to the console of the pump. Deflation is timed to the opening of the aortic valve, so during systole, while inflation matches to the closure of the aortic valve, during diastole. In that way, the deflation in systole reduces postload, very important factor in pediatric practice, and increases ventricular contraction performance, while inflation in diastole increases diastolic aortic pressure and coronary perfusion.[29]

However, since the beginning, some really big issues came out from the adaptation of IABP to pediatric use: [29]

- The huge elasticity of the pediatric aortic wall may alter the diastolic forces and make IABP support uneffective for the pediatric patient.
- The high heart rate and the high incidence of arrhythmia in pediatric patients can make difficult the timing of inflation and deflation.
- The incidence of complications of the IABP in children was very high, due to difficult insertion of the device in small vessels as children's ones are.

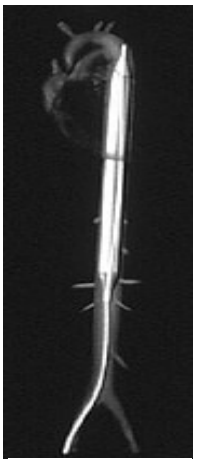


Figure 13 IAPB positioned at x-ray

The first experiences with pediatric use of IABP [28,30] showed a very high rate of complications and mortality, but despite that, several more recent studies, [31,32,37] also in in-vitro models[33,36] and animal models[34,35,36] have shown, that thanks to the progress in technology, IABP use can be feasible and effective in term of diastolic augmentation and postload reduction, with a better hemodynamic, for selected cardiac pediatric patients of all ages undergoing refractory low cardiac output state, with an acceptable risk profile.

But we have to remember that in right ventricular failure, the case often observed in congenital heart diseases, common cause of heart failure in pediatrics, IABP is ineffective. On the contrary, myocardial ischemia, for which an IABP can be useful, is a really uncommon cause of heart failure in pediatrics. So, IABP seems to be useful particularly in children with mild left ventricular dysfunction, but more severe cases require more likely the use of a specific LVAD.[63]

3.5 The TandemHeart®

Commento [Office1]: hai trovato leteratre su casi pediatrici?

The TandemHeart® is a percutaneously placed left atrium-femoral artery bypass system composed by a transseptal cannula (21 fr) inserted in the left atrium, arterial cannulae (from 9 to 17 fr) inserted in the femoral artery, and a centrifugal electromagnetic blood pump which can deliver blood flow rates up to 4.0 L/min with a maximum rotor speed of 7500 rpm (figure 14). The cannulae are connected to the pump, which is connected to the controller system that provides control of flow rate and impeller speed. It provides unloading of the left ventricle, so it can be considered a LVAD.

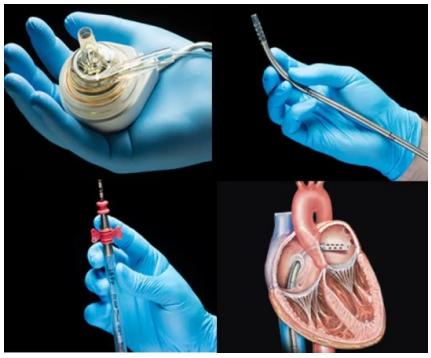


Figure 14 TandemHeart components: the pump, the transseptal cannula, the arterial cannula and the positioning

A pediatric version of this pump has been developed [39,42], with several important differences respect to the adult version (figure 15): pediatric model has a larger impeller diameter and smaller gaps between the upper housing and the impeller respect to the adult pump. Then, the priming volume of the pediatric pump is 4 ml, whereas it's 7 ml for the adult one. Furthermore, new cannulation techniques were investigated as alternative to the standardized femoral cannulation used to place the adult TandemHeart system to reach the left atrium, through the right internal jugular vein and through hepatic vein (transhepatic cannulation): thanks to the shorter distance to the left atrium and larger size of hepatic vein, design of specific pediatric cannulae with adequate flow rate was allowed.[43]

Commento [MV2]: Ecco i reports che ho trovato sul tandem Heart pediatrico

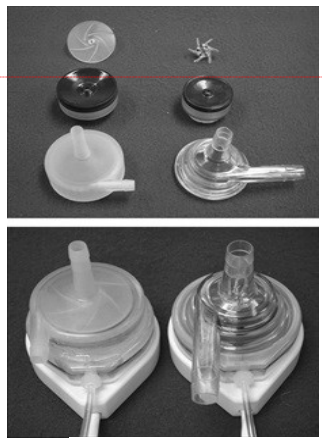
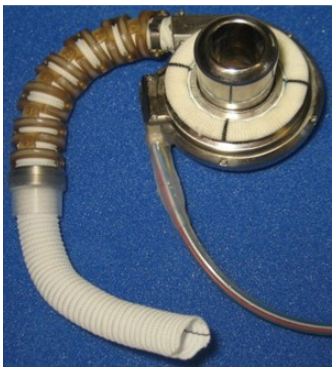


Figure 15 pediatric and adult TandemHeart pumps

Regarding the use of this type of device in small children, due to the poor experiences and data present in literature, basically case reports,[38,40,41,42] and in

vitro models[39], it's hard to define if this type of device can be safely used in children keeping the rotor at the minimum speed of 3500 rpm (the working range in the adult model is 3500–7500 rpm). This issue, together with the cannula size, may limit the use of TandemHeart in children, and more studies are needed to determine the safety of this kind of device for pediatric use. This could allow an off label use of this technology in smaller children with heart failure, for which ECMO is often the only solution for short-term ventricular support, but with all the issues discussed in the dedicated paragraph, as a valid aternative to ecmo or pulsatile devices.

3.6 The Medtronic HeartWare™ (HVAD™)



Medtronic produces a very promising device in pediatric scenarios: the HeartWare™ (HVAD™) intrapericardial continuous flow pump. Even if this device is born as a LVAD, some case reports, [53,54] a multicenter study [51] and also a retrospective study[52] has shown its use in children needing biventricular support, placing it also in the right ventricle, challenging with a very rare and risky procedure. The biggest issue encountered using this kind of device in children, in both cases, was bleeding, resulting in tamponade and need for reoperation. In all these studies, the limit encountered was that the implantation seemed to be safe only for patients weighting more than 20 kg. But despite this, more recent experiences[56,57,58] has shown that HeartWare™ implantation in adolescents can be successful as a bridge to transplantation. Even if the morbidity is not trascurable as well, it seems to be comparable with that seen in adult patients. This device now is out of commerce.

3.7 The HeartMate devices series

The heartMate™ by Abbott is a compact centrifugal continuous-flow LVAD. There are currently two models: the HeartMate II™, mounting an axial flow pump, placed in a surgically created subcutaneous pocket; and the HeartMate3™, intrapericardial device with a full MagLev technology centrifugal pump; widely used for both bridge and destination therapy in adult patients. The HeartMate3 is usually implanted in children by median sternotomy, while alternative routes, for example a less invasive lateral sternotomy, are possible only in adults. In children the outflow graft is connected to the ascending aorta, while in adults it can also be connected to the descending aorta. The poor experience in pediatric use has evidenced the need to investigate more the use of this devices in children as an alternative to ECMO and other VADs. It's a very compact device, so it has a huge potential in pediatric use.

Figure 16 A : HeartMate II B:HeartMate 3

The biggest issue encountered to implant the Heart Mate in small patients is the small space in the thoracic cavity and the potential compromission of the pump position when closing chest after implantation. [46]

Several case reports[46,48,49] and multicenter studies[47]

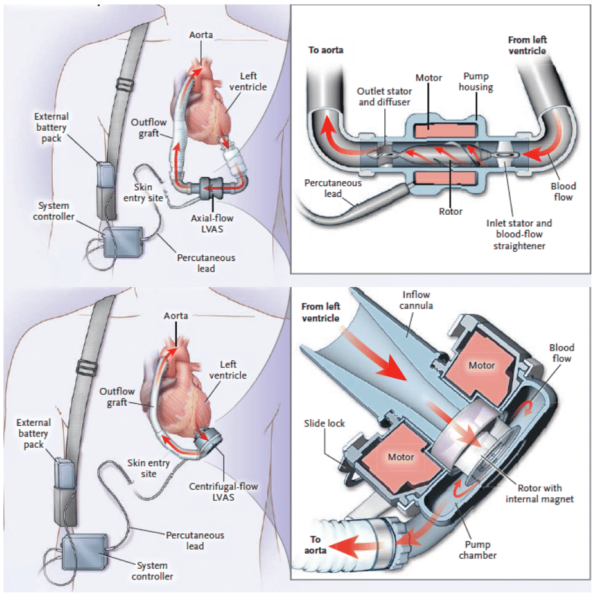


Figure 17 HeartMate II and HeartMate 3™ Left Ventricular Assist Device functioning.

showed pediatric patients successfully implanted and supported by HeartMate devices, indicating its appropriateness of use in bigger children and small young adults, and showing that the device size is not a limitation.

3.8 The Jervik 2000

Figure 19: infant, pediatric and adult Jervic 2000 pumps

The Jarvik 2000 LVAD device is an electromagnetically-powered miniaturized intraventricular continuous axial-flow valveless LVAD based on an impeller pump. The device is placed directly in the apex of the left ventricle and the dacron outflow graft draws blood into the descending aorta. The pediatric sized pump is an adaptation from the adult Jarvik 2000 model (in figure 19 the different models). The pediatric Jarvik 2000 can deliver a blood flow from 1.4 to 2.5 L/min with impeller speed from 10,000 to 14,000 rpm. However, the biggest issue encountered in this device was bearing thrombosis, responsible for device malfunctioning in most cases. To overcome this issue, the initially used pin bearings have been replaced with conical bearings. The second version resulted to be even less hemolythic[61]. The first in vivo animal studies [59,60,61] and more recent case report on real patients[62,65] demonstrated the potential of this device to give children circulatory support: the combination of ease of implantation, durability, small size and biocompatibility make pediatric Jervik 2000 an interesting assist device for children unable to tolerate larger LVADs. In figure 20 is shown how the device can be placed,[63] with th outflow tract both in the ascending or descending aorta. In addiction to this, we have to remember and take in count that most pediatric patients need a biventricular support, but this system can be successfully used as

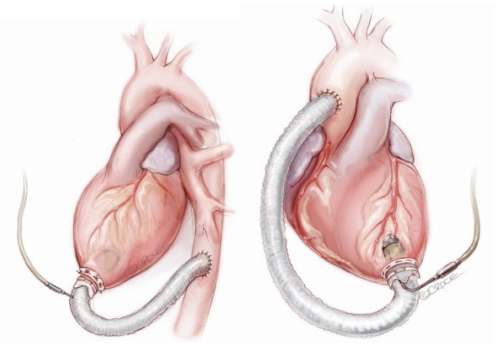


Figure 20: positioning strategies of Jervik 2000 device: outflow tract in descending (A) or ascending (B) aorta

a permanent ventricular assist device or bridge to transplantation or recovery in children needing only left ventricular support.

3.9 The MEDOS-HIA ventricle family

The MEDOS-HIA VAD system, produced by HIA in Germany, is a compact, pneumatic pulsatile paracorporeal assist device, on the market since 1994, used in both pediatric and adult patients. [66] There are various sizes of the artificial ventricles: three left sizes of 10, 25 and 60 mL of volume, smaller ventricles, of 9, 22.5 and 54 mL, are designed for right ventricular support or biVAD used together with the left ones (Figure 21). They are all made of transparent polyurethane. Also the cannulae of the appropriate size are available, suitable for neonates to large adults, and there are available for LVAD, RVAD or biVAD. Into the artificial ventricle the blood flow is straightened by a three-leaflet polyurethane bulb valve directly incorporated in the device. In fact, in small children requiring small ventricles but high pump rates, mechanical valves are usually undesirable for their closing-opening properties. Several single center experiences and case reports in the last decades [67,68,69,70,71,72] showed that short-to long term support or bridge to transplant can be successfully performed in children, with careful monitoring and following the correct matching size of the device.

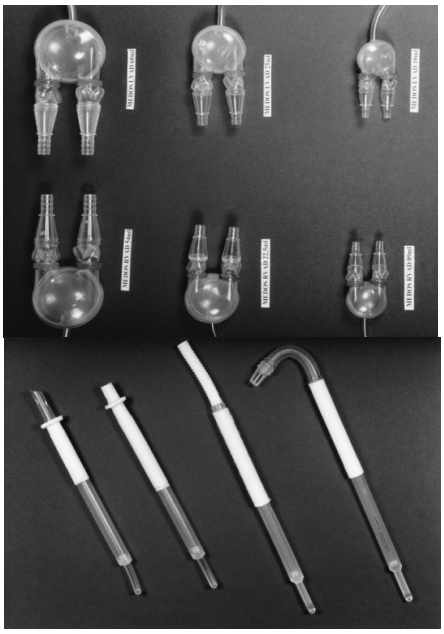


Figure 21: MEDOS ventricles and cannulae in their vasious sizes

3.10 The Syncardia ™ total artificial heart

Figure 22: The syncardia TAH in the two sizes

The Syncardia™ Total artificial heart (TAH) is the only TAH approve d by FDA in the world. It is a pneumatic pulsatile device replacing totally ventricular function and all the four cardiac valves. It's able to provide blood flow of more than 9L/min. It is actually available in two sizes, 50 cc and 70 cc (figure 22), and can be used in patients with sufficient chest size as bridge to heart transplant or destination therapy, however the first design needed to be scaled to fit also the smaller patients. In fact, the patient's pericardial space must be sufficient to accommodate the device without causing venous compression, issue which can inficiate the device filling. Figure 23 displays the surgical steps necessary to implant a Syncardia TAH in the patient.

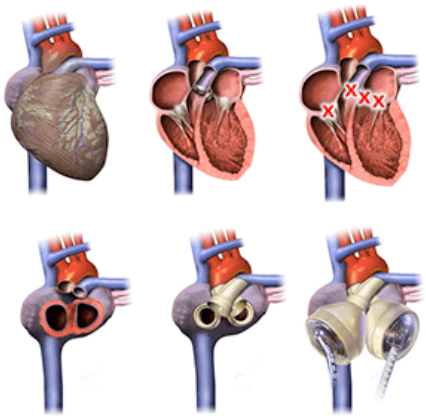


Figure 23: the implantation procedure steps for syncardia TAH

The number of pediatric patients implanted with TAH in the last times has increased [78,79,80,81], and the experience, started as case reports [82,83] and then extended, showed that the outcomes in children with both the sizes of TAH were similar to the ones in adult patients requiring TAH or other type of biventricular support.

4 Comparison of the outcome for the techniques

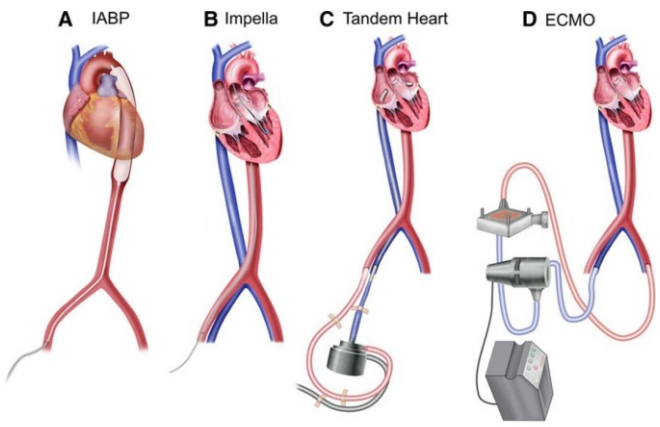


Figure 24: overview of the different technologies

Each of these technologies has its pros and cons, so an overview of advantages and disadvantages of the various possibilities is needed. A single-center retrospective review, comparing temporary cfVADs and ECMO support in pediatric patients with less than 19 years with progressive acute heart failure[2] evidenced that temporary cfVAD can be used to support pediatric patients for a longer time compared with ECMO, which makes it a valid option to durable VAD, bridge to recovery, bridge to decision or transplant. In this study thirteen patients underwent temporary cfVAD, and 11 ECMO, with similar indications. Median cfVAD support was 20 days whereas it was 9 days for ECMO. Primary outcomes for cfVAD patients were: one decannulated with recovery, six transplanted, six died. For ECMO instead: five decannulated with recovery, three transplanted after conversion to durable VAD, and three died. No patients were transplanted directly from ECMO, but some patients on ECMO were transplanted after conversion to VAD (temporary or durable). Other advantages of temporary cfVAD include its ease of handling and implantation, lower priming volumes respect to ECMO, less complications, possibility to integrate the oxygenator in the circuit, approval for use without being in list for transplant, and reduced cost. [3-8]

Another single centre retrospective study[6] showed that cfVADs can be a successful bridge for most pediatric patients to recovery, long-term device or transplant, with a good complication and risk profile, so although these devices were designed to provide a short-term support, also a longer-time support is

possible, and may be an interesting alternative for that patients who are not candidable to long-term devices.

On the other side, literature reports that ECMO for long time has been the standard of care for short-term mechanical circulatory support in pediatric patients, but the limits of ECMO as a bridge modality, mostly due to an increasing rate of fatal complications after about 14 days of use, have been well described in literature and already mentioned in the introduction. In addiction is necessary to remember that ECMO requires sedation, mechanical ventilation, and necessity to keep the child bedbound for all the duration of the treatment. It is unknown if the newest temporary circulatory support devices can give to children a significant survival advantage compared to ECMO. The objective was to compare ECMO and new TCS devices in children as a bridge to transplant. Also in this study[7] it was confirmed that, compared with ECMO, TCS devices last longer, and more importantly, the survival to transplant and the overall survival rate were superior.

Furthermore, a multi-center American retrospective study[9] investigated the clinical outcomes for 73 children supported with the Berlin Heart EXCOR as a bridge to transplant, in 17 different American centers. Both LVAD and biVAD were tested. The significant issue was that approximately 33% of patients were already supported with ECMO until EXCOR was implanted. Also this experience showed and confirmed the safety and efficacy of the EXCOR device ad a bridge to transplant in pediatric patients. A further retrospective comparison study by Iamamura et al.[10] investigating the outcomes for pediatric patients receiving mechanical support with ECMO or the Berlin Heart EXCOR cfVAD demonstrated that the EXCOR device allows longer support time and a better overall survival. In addition, neurological complications, associated with both approaches, were less often fatal in patients who received the VAD. Furthermore, an important issue to keep in mind, is that ECMO provides a biventricular support (even when the right ventricular function is preserved), instead the EXCOR VAD device gives the possibility to decide to provide both univentricular or biventricular support, decision which is not always simple and linear to take.

In addition, we have to keep in mind that pediatric VADs, or adaptation of adult models to children, have significant differences in needs and functioning respect to the adult ones: they have to support a wide range of different sizes from newborns to adolescents, they have to follow circulatory demand increasing with growth, counting for the anatomophysiological variability of congenital heart diseases. In conclusion, literature showed that VADs are a very good option for temporary support in children: in comparative studies[73,74], it has been showed that the Thoratec device can be easilly and safely placed in small patients with large hearts, which can accommodate the available cannulae; while the Berlin Heart and Medos devices already have a selection of pediatric designed ventricles with small volumes. All these systems can be used successfully in the pediatric population, with less complicances and a better survival than ECMO, outcomes confirmed also by the First analysis of the Pediatric Interagency Registry for Mechanical Circulatory Support (PediMACS).[75]

Device	Size Restrictions	Duration of Support	Type of Support	Pump Flow	Approved for Use by US FDA	Pathway of US FDA Approval	Labeled Excluding Use in Children	Studied Prospectively in Children
Temporary								
ECMO	None	days	Biventricular	Continuous	Yes	510K	No	No
CentriMag	None	Days–weeks	Univentricular or biventricular	Continuous	Yes	510K	No	No
Rotaflow	None	Days–weeks	Univentricular or biventricular	Continuous	Yes	510K	No	No
TandemHeart pVAD	N/A	Days	Univentricular	Continuous	Yes	510K	No	No
Impella 2.5/5.0	N/A	Days	Univentricular	Continuous	Yes	510K	No	No
Durable								
Berlin Heart EXCOR	Wt >3 kg	Months–Years	Univentricular or biventricular	Pulsatile	Yes	HDE	Labeled for children	Yes
HeartWare HVAD	Wt >*15 kg	Years	Univentricular or biventricular	Continuous	Yes	PMA	No	No
HeartMate II	Wt >*30 kg	Years	Univentricular	Continuous	Yes	PMA	No	No
Syncardia Total Artificial Heart	BSA >1.7 m^2	Years	Biventricular	Pulsatile	Yes	PMA	No	No

BSA indicates body surface area; ECMO, extracorporeal membrane oxygenation; FDA, Food and Drug Administration; 510K, pathway of approval based on demonstrating equivalence to predicate device; HDE, humanitarian device exemption; HVAD, PMA, postmarket approval; pVAD, percutaneous ventricular device; and Wt, weight.

Table 3: overview of the state of art for FDA approval and studies about VADs in children

Table 3, from the US FDA Orphan Devices Program,[44] resumes in an overview the features, the state of art for FDA approval and studies for all the different mentioned devices applied to children, as well as size restrictions encountered using them in children. Of course, as seen until here, both pulsatile and cfVADs

can be used in children, but paracorporeal pneumatic pulsatile pumps are mostly used in smaller children, while for larger patients intracorporeal continuous flow devices, as HeartMate LVAD, are preferred. So the options for larger children and teenagers are growing really fast, but, for newborns and infants, the best option for mechnical support is still restricted to the EXCOR Berlin Heart, that, as mentioned in the dedicated paragraph, is the only device approved entirely by FDA appositely for pediatric use.[45,50]

Table 4, result of a very complete review of all the available options for children circulatory support,[64] summarizes important technical details about all the mentioned VADs, ECMO and IABP, such as the position of the device, the kind of support given, the duration, cannulation site, type of flow and power source; helping to guide the choice of the device, which is peculiar for every single pediatric patient.

Type of device	Intraaortic balloon pump	ECMO	Centrifugal pump	Berlin Heart	Medos	Thoratec	Novacor	HeartMate	Abiomed	Jarvik 2000
position	intraaortic	external	external	external	external	external	external	external	external	internal
ventricular support	left	both	left, right or both	left, right or both	left, right or both	left, right or both	left only	left only	left, right or both	left
pediatric application	yes	yes	yes	yes	yes	yes	no	yes	yes	no
average duration	short	short	short	short	short	Intermediate long	long	long	intermediate	long
flow	pulsatile	non-pulsatile	non-pulsatile	pulsatile	pulsatile	pulsatile	pulsatile	pulsatile	pulsatile	non-pulsatile
power source	pneumatic	electric	electric	pneumatic	pneumatic	pneumatic	electric	electric or pneumatic	pneumatic	electric
Cannul. site	peripheral	peripheral arterial and venous	central or peripheral	central	central	peripheral or central	central	central	central	central
native ventricle	remains	remains	remains	remains	remains	remains	remains	remains	remains	remains
Anticoag.	not necessary	yes	not necessary	yes	yes	yes	yes	no	yes	no
patient ambulation	no	no	no	no	no	yes w/assistance	yes	yes	no	yes
patient discharge	no	no	no	no	no	no	yes	yes (electric)	no	yes

Table 4: overview of the technical details of the available VADs

In this recent review by Moisă et al[76] there is an updated overview of literature about past experiences with VADs approved by FDA for pediatric use, exploring the main available and tested devices in terms of

implant indication, adverse effects, and outcomes. As it had been found in the already mentioned less recent experiences, it has been confirmed that the main adverse effects of these devices were thromboembolism, infection, bleeding and hemolysis, which occur at a still hihg rate.[75] Table 5, result from the same review, resume advantages and disadvantages of every device.

	Type of VAD	Advantages	Disadvantages
1	Berlin Heart Excor	It constitutes a pulsatile pump implanted outside the chest and attached to the atria, left ventricular apex, and major vessels. It could serve as a bridge-to-transplant therapy for children of all ages.	Several disadvantages should be accounted for, including the risk of bleeding (44%), thrombotic (21%), and infectious events (46%), implantation and explantation issues, the need to exteriorize the cannula, and financial problems [9].
2	Medos HIA	It constitutes a compact, extracorporeal, pneumatically driven system for left, right, or biventricular support. Pumps are available in different dimensions and can be used in children regardless of weight and height.	Risk of bleeding events which could require re-intervention and risk of infections (50%) [11
3	Thoratec	These pumps are magnetically levitated, have low prime volumes and negligible hemolysis, and are permitted for 30 days by the Food and Drug Administration.	Potential adverse events include infectious bleeding, thromboembolic complications (27%) prolonged ventilation, neurologic events, and system malfunction [15]. Also, these devices require anticoagulation control.
4	HeartMate III	It constitutes a compact centrifugal ventricular assist device. It was successfully used as a bridge-to-transplant therapy in adolescents. The device carries a low risk of thrombosis and stroke.	Potential adverse events during follow-up include infectious (11.4%) and bleeding complications (11.4%) and arrhythmias (8.6%) [30].
5	Impella	It constitutes a catheter-based, miniature ventricular assist device, which could be placed by retrograde femoral artery access into the left ventricle across the aortic valve.	The device could be used only for short-term ventricular support. Potential issues should be addressed: vascular access site complications, purge failure, and bleeding events (5.2%) [8].

Table 5: advantages and disadvantages of VADs

Furthermore, also bridge-to-bridge strategies may be needed, in order to increase the survival on the transplantation waiting list. So, the outcome of children with heart failure who received a single support strategy with those who received multiple devices was investigated and compared in a retrospective study.[77] The result was that bridge to transplant with multiple strategies seemed not to influence the outcome respect to use a single strategy. However, clearly, children who received more than one support modality were supported for longer time.

5 The Padua experience

At the university Hospital of Padua a retrospective study on children admitted to the center for heart failure between 2012 and 2022 was performed. The aim of the study was to show, once again, the VADS are safe and effective to treat heart failure in children, and they are a good way to take time waiting for the transplant but also as a final destination therapy. The Padua experience however focused only on intracorporeal LVADs, while all the paracorporeal ones were excluded from the study. In fact the children included in the study received a HVAD or HeartMate device, both, as described before in the dedicated paragraph, intracorporeal devices.

But also, another important aim of the study, was to show the importance of a careful pre - operatory planning trough TC scan and modeling, to choose the more appropriate device and to plan carefully its surgical positioning.

6 Materials and methods

This is a retrospective single-center observational study involving all the patients with less of 18 years of age, admitted to our center for ESHF from 2012 to 2022. The review of medical records was approved by our institutional Ethics Committee for clinical investigation (protocol nr. 59004), and the patient's informed consense was obtained. Patients were included in the study regardless for the ESHF etiology, with LVAD implantation as bridge-to-candidacy, bridge-to-transplant, or destination therapy. The study included only patients implanted with third generation, intracorporeal LVADs, paracorporeal devices were excluded.

Preoperative patient's data included demographics, etiology of ESHF, clinical characteristics and imaging (echocardiography, cardiac catheterism or thoracic computed tomography with contrast media).

The outcomes included post-operative complications, early death (less than 30 days from the surgery), or late death (more than 30 days from the surgery or after hospital discharge).

Follow-up data included clinical status (New York Heart Association functional class), occurrence of either transplant (HTx) or adverse events (AEs): death, infective complications (e.g. exit-site infection, systemic infection, etc.), thrombotic/hemorrhagic complications, neurological events or need for reintervention (surgical or not).

We described the continuous variables, as median (interquartile range, IQR), whereas the discrete variables were described as numbers (with percentages, %). Baseline, intraoperative and postoperative outcomes were collected and compared. Statistical analysis was performed using the non-parametric Mann-Whitney U test.

All the patients with a BSA greater than 1.2 m^2, having so an expected small thoracic cavity, underwent a preoperative CT to evaluate their chest dimensions.

The CT scans were performed using a 320-slice CT scanner (Toshiba Aquilion ONE; Canon Medical Systems, Otawara, Japan). Gantry rotation time was 350 msec, the slice thickness was 0,5 mm, and the recon increment was 0,25 mm. Tube potential was generally low-dose (80 kV) for scanning infants and children through the first decade of life, while a 100 kV dose was used for overweight children or adolescents, especially if there was the need to examine subtle details such as coronary artery stenosis. Usually, a biphasic injection protocol (contrast medium followed by saline solution) was adopted, acquiring a single contrast scan (only arterial phase) or a biphasic scan protocol (both the arterial and venous phase), by using automatic bolus tracking. Automatic exposure control (SURE exposure 3D, Toshiba Medical Systems) and iterative reconstruction (AIDR3D standard, Toshiba Medical Systems) were used. Those patients requiring a detailed evaluation of structures prone to cardiac motion artifacts and those requiring functional assessment were scanned using ECG gating. All the scan data were transferred to an external workstation (Vitrea2 FX version 6.3, Vital Images, Plymouth, MN, USA) providing multi-planar reformation (MPR), curved planar reformation (CPR), volume rendering technique (VRT), cine-view and semiautomatic vessel analysis system to assess the vasculature.

More recently, a 3D reconstruction of the heart and chest cavity was performed for younger children (BSA less than 1.2) and virtual fitting and surgical planning were performed using separate 3D models for the rib cage, heart chambers and the devices considered for implantation. Also, simulations of different LVAD positions in the left chest were performed, in order to optimize the LVAD location.

In some special cases, airways and main vessel models were also generated and summed to allow a complete spatial reconstruction of the surgical site and optimal outflow graft path planning.

The reconstructions were made using the Mimics inPrint 3.0 software (Materialise NV, Leuven, Belgium). For each case, a complete chest CT scan of the patient was imported and the various structures, differentiated by density,

different contrast enhancing or spatial location, were segmented separately. The 3D models of the pumps were generated using CT scans of previously implanted patients and their dimensions were confirmed to be accurate by comparing virtual measures with the physical dimensions as declared by the manufacturer's technical specifications.

Finally, all the models were combined together and the virtual fitting was carried out by freely moving and rotating the pump and its fixed metal outflow to the apex of the left ventricle, while carefully controlling the inflow cannula depth within the ventricular wall and the clearance between the internal surface of the ribs and the device itself.

7 Results

Among the 31 patients who underwent mechanical assist devices implantation between 2012 and 2022, 11 patients (M/F=9/2, median age, 13.9 -IQR 10.7-14.7, range 10.5-16) received 11 third generation intracorporeal LVADs. Their median body surface area was 1.42 m2 (IQR 1.06-1.68). Preoperative characteristics of the patients, mentioned before, are described in detail in Table 1. Etiology of ESHF was dilated cardiomyopathy in all the patients, but one of them (biventricular heart failure in a 12-year-old boy with corrected transposition of great arteries and pulmonary atresia, after multiple surgical procedures during infancy).

The median preoperative left ventricular ejection fraction (LVEF) was 24 % (IQR 15-26). One of the patients were on intravenous inotropic drug infusion (10/11 patients, 90.9% didn't need it). The INTERMACS profile was 3 in five patients (45.5%), 2 in two patients (18.2%), and 1 in three patients (27.3%).

Preoperative feasibility assessment included a CT scan in all, and 3D reconstruction with LVAD virtual fit simulation in 3 of the 4 patients with BSA<1.2 m^2.

The LVAD was implanted as a bridge-to-transplant in 7 cases (63.6%), as a bridge-to-candidacy in 3 (27.3%), and as destination therapy (DT) in a 14-year-old patient with Duchenne's syndrome. All three patients implanted with a bridge-to-candidacy strategy displayed an elevated pulmonary arteriolar resistance (12.67 WU, 9.58 WU, and 6.76 WU, respectively).

Three patients (27.3%) were on mechanical circulatory support before LVAD implantation: 2 with femoral-femoral veno-arterial extracorporeal membrane oxygenation (VA-ECMO), one with paracorporeal LVAD configuration through apical cannulation (apical-femoral configuration), after an initial VA-ECMO. Four of the patients (36.4%) were on mechanical ventilation preoperatively.

Seven HeartWare (HVAD, Medtronic, Minneapolis, MN) (63.6%) were implanted between 2012 and 2020, while 4 HeartMate 3 (HM3, Abbott Inc., Chicago, Illinois, Il) (36.4%) were implanted in 2022. The surgical LVAD implant was performed through median sternotomy in all patients except one 15.9-year-old boy, (BSA 1.93 m2) who underwent the device implantation through a bi-thoracotomic access. A temporary right ventricular mechanical support was necessary in 2 patients, for 3 and 4 days respectively. The median time of post LVAD mechanical ventilation was 3 days (IQR 1-3), despite 4 patients (36.4%) required it for more than 3 days.

The most common postoperative complication resulted to be bleeding, requiring surgical re-exploration (36.4%), with cardiac tamponade in one case only. Major infectious complications occurred in 2 patients (18.2%), that were successfully treated with antibiotic therapy.

In-hospital mortality occurred in a 12.4-year-old patient affected with complex congenital heart disease, who underwent multiple surgeries, who experienced a first cardiac arrest, requiring resuscitation and emergency ECMO implantation before LVAD implant, and then a second episode of low cardiac output because of bleeding and cardiac tamponade. Despite the recovery of cardiocirculatory stability, a severe cerebral anoxic damage led to an irreversible comatose status with care withdrawal on postoperative day 119. All the intra-operative details and post-operative complications are reported in detail in Table 2.

Among the patients who survived, 4 of them (36.0%) were transplanted before being discharged from the hospital (median LVAD-to-HTx time 23.0 days , IQR 8.8-44.0). The remaining 6 patients were discharged after a median hospital stay of 34.5 days (IQR 30.0-40.5), under anticoagulation therapy with fondaparinux in 3 cases, warfarin with antiplatelet therapy (Clopidogrel in 2, acetylsalicylic acid in 1) in the others. The target INR ranged between 2.5 and 3.5.

After hospital discharge at a median follow-up of 182.5 days (IQR 78.8-613.8), there were no late death or other complications in the remaining 6 children; however 3 of them had driveline exit-site infections, that were successfully

treated. Four patients underwent a successful heart transplant after 42, 110, 255, and 1387 days from LVAD implantation. Two of the patients are still on mechanical support, doing well at home, following regular follow-up evaluations, after 13.3 and 4.4 months, respectively, under treatment with warfarin for pump thrombosis prophylaxis.

Overall, all long-term survivors with a bridge-to-transplant indication (6 patients out of 7, 85.7%) underwent a successful transplant, and all patients with a bridge-to-candidacy for pulmonary hypertension normalized the pulmonary resistances and after that underwent a successful transplant. The last patient with Duchenne syndrome showed a stabilization of the neurological problem, with excellent clinical conditions. Thus, he was finally listed for the transplant, and after 1387 days of uncomplicated HVAD support he also underwent a successful transplant.

Table 3 summarizes the characteristics of patients implanted with the Heart Ware HVAD and HeartMate 3. There were no statistically relevant differences between these two groups.

8 Discussion

Commento [Office3]: La discsuione è un po povera.
Devi arrichhire la discussione, soprattutto sugli effetti e vantaggi della possibile domiciliazione a casa, invece che stare in Ter Int, o sopedale; , e le tecniche di CT guided Virtual fitting per capire se HM3 è compatibile con le dimensioni dei bambini

The results that emerged by from the Padua experience are very promising for the treatment of pediatric heart failure and in line with the results found in literature for the same kind of devices. The implantation of intracorporeal devices for cardiac support demonstrated to be safely feasible in children: in fact, after the procedure, only one of the patients needed inotropic support, and only two of them needed an additional right ventricular support, confirming that the procedure can give very effective results in the treatment of pediatric heart failure.

Also, the post-operative complicances, confirmed to be bleeding and major infections, so that is the point where there is still work to do, but as seen before, but as seen in the results, these complicances have been successfully managed.

The post-procedure mortality data are also promising, and resemble the results found in literature and discussed before: in the whole Padua study, it occurred in only one case among all the patients taking part to the study, taking also in account that it was a very complex case, undergoing multiple surgeries, and encountering severe complications itself.

Furthermore, also the late death results showed to be optimal, none of the patients underwent late death or major complications after hospital discharge, when presenting to the follow-up screenings.

The study analyzed intracorporeal LVAD implantation as bridge to transplant (7 cases) bridge to candidacy (3 cases and destination therapy (1 case, the boy with Duchenne MD), and the procedure was successful for all three options: the children who were indicated for transplant underwent a successful surgery with an overall survival of almost 86% (6 out of 7); the three patients with bridge to candidacy indications also underwent successful transplant after normalizing their clinical conditions, and also the boy with Duchenne MD, after more than 4 years of HVAD support, was finally listed for the transplant.

A really important result that emerged from the study, and also from the other similar studies in literature, is that this kind of approach reduced ICU stay and the days of hospitalization, with all the important advantages that it can represent for the patient, especially for a child, for which is fundamental to have a fast and better recover, a shorter hospital stay, and resume a "normal" life as soon as possible. Another important goal that has been reached and that has to be improved even more, is the reduction of morbidity and mortality of the procedure.

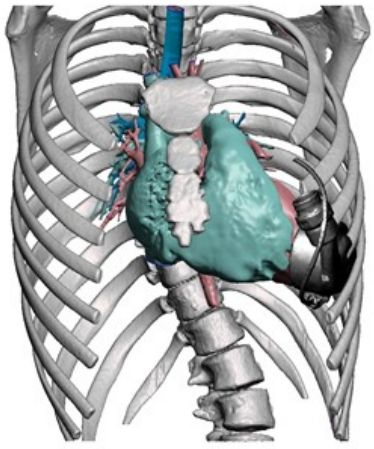
All these promising results confirmed another time that Intracorporeal LVADs can be an interesting alternative for pediatric cardiac support, with acceptable morbidity and mortality and adequate profile risk.

Furthermore, the Padua study demonstrated that a huge contribution to that good results is given from an adequate pre-operative study, performed with TC scan in all the patients of the study and also 3D modeling for some of them, helping to prepare the surgery as better as possible and prevent and avoid the most known complicances. 3D reconstruction with LVAD virtual fit simulation has been performed in fact in 3 of the 4 patients participating in the study with BSA<1.2 m^2, to see if the device (in that case it was HM3) was fitting with the child's dimension of the thorax. Figures 25 and 26 show an example of CT-guided 3D virtual fitting modeling performed to see if the device has suitable dimensions for the patient. Clearly, choosing the device with a suitable dimension is a big issue, conditioning the result of the surgery, so is important to have the possibility to use these simulations to make the proper choice.

Commento [MV4]: Mi sembra che Irene avesse delle references a riguardo, si potrebbe inserirle?

Commento [MV5]: Vantaggi per il bambino di avere degenza più breve e recupero migliore (spero non ci siano troppe ripetizioni

Commento [MV6]: Qui ho ripreso i vantaggi del 3d fitting ed inserito le immagini che mi ha allegato



Figures 25 and 26: example of 3D guided virtual fitting for HM3 device

Putting together the advantage of a shorter and better convalescence, the possibility to know in advance, thanks to the modeling, if the device can be suitable, and the good profile risk, these intracorporeal devices are a very valid alternative to treat pediatric heart failure.

9 Conclusions

The Padua experience, in line with the previous literature, also showed that continuous flow LVAD implantation can be a safe and feasible option also in pediatric patients with a BSA less than 1.5 m^2. Thanks to the current advance in cardiac imaging technology, a comprehensive preoperative assessment and virtual fitting simulation with a 3D reconstruction of the device In situ and the patient's chest can effectively help to extend its application even to the youngest children, allowing to reduce morbidity and mortality among pediatric patients listed for heart transplantation.

Tables

Table 1. baseline patient's characteristics.

Demographics	
Age (years)*	13.9 (10.7-14.7)
Gender (male) §	9 (81.8)
Weight (kg) *	47.0 (28.0-65.0)
Height (cm) *	154.0 (140.0-163.0)
Body Surface Area (m2) *	1.42 (1.06-1.68)
Heart Failure Etiology	
Dilated cardiomyopathy §	10 (90.1)
Primitive idiopathic	4 (36.4)
Familiar Restrictive	1 (9.1)
Carvajal's syndrome &	1 (9.1
Iatrogenic (anthracycline) &	1 (9.1)
Duchenne's syndrome &	1 (9.1
Post-myocarditis &	1 (9.1
Non-compaction cardiomyopathy §	1 (9.1)
Post-surgical correction of CHD in infancy §	1 (9.1)
Echocardiographic data *	
Left ventricle ejection fraction (%)	24.0 (15.0-26.0)
Implantation strategy §	
BTT	7 (63.6)
BTC	3 (27.3)
DT	1 (9.1)
BTC: Bridge-to-candidacy; BTT: Bridge-to-transplant; DT: destination therapy. *: median (interquartile range); §: number (%); &: percentage relative to the total number of dilated cardiomyopathy	

Table 2. intraoperative details and postoperative outcomes.

Intraoperative	
Heartware HVAD implantation	7 (63.6)
HM3	4 (36.4)
Access: full median sternotomy	10 (90.9)
Outcomes	
Post-surgery intubation time (days)*	3 (1-3)
In-hospital mortality §	1 (9.1)
30-day mortality §	0 (0.0)
Neurological complication §	3 (27.3)
Major Neurological complication (post-anoxic coma)	1 (9.1)
Temporary RVAD implantation §	2 (18.2)
Bleeding requiring surgery §	3 (27.3)
Infective complication §	5 (45.5)
Major (sepsis, pneumonia)	2 (18.2)
Minor (uncomplicated driveline exit-site infection at follow-up)	3 (27.3)
HM3: HeartMate 3; HVAD: HeartWare VAD; RVAD: Right ventricle assist device. *: median (interquartile range); §: number (%)	

Table 3. HVAD and HM3 comparison of preoperative characteristics, intraoperative details, and postoperative outcomes.

	HeartWare HVAD n = 7	HeartMate 3 n = 4	p value
Preoperative			
Demographics			
Age (years) *	14.3 (10.7-14.7)	12.4 (10.8-15.4)	0.927 #
Gender (male) §	6 (85.7)	3 (75.0)	0.618 ^
Weight (kg) *	47.0 (26.5-64.9)	50.5 (29.0-82.5)	0.788 #
Height (cm) *	150.0 (140.0-163.0)	159.0 (144.5-163.75)	0.527 #
BSA (kg/m^2) *	1.42 (1.06-1.68)	1.51 (1.10-1.86)	0.788 #
Implantation strategy §			
BTT	4 (57.1)	3 (75.0)	0.701 &
BTC	2 (28.6)	1 (25.0)	
DT	1 (14.3)	0 (0)	
Intraoperative §			
Access: full median sternotomy	7 (100.0)	3 (75.0)	0.364 ^
Outcomes			
Post-operative RVAD §	2 (28.6)	0 (0.0)	
Post-surgery intubation time (days) *	4 (1.0-11.0)	2.5 (1.25-3.0)	0.412 #
Admission-to-implantation time (days) *	28.0 (12.0-43.0)	13.5 (9.3-17.8)	0.164 #
Discharged Home on LVAD §	3 (42.9)	3 (75.0)	0.571 #
BTC: Bridge-to-candidacy; BTT: Bridge-to-transplant; DT: destination therapy; LVAD:			

Left Ventricle Assist Device; RVAD: Right Ventricle Assist Device.
*: median (interquartile range); §: number (%);^: Fisher's ExactTest; #: Mann-Whitney U test; $: Pearson Chi-Square

Pt	**Age (years)**	**Weight (kg)**	**BSA (kg/m²)**	**ESHF etiology**	**Baseline LVEF (%)**	**Type of LVAD/ Implant Strategy**	**Surgical Access**	**Complication**	**Status at follow-up**
1	10.5	26.5	1.06	Non-compaction DCM	10.0	HVAD/ BTT	Median sternotomy	*None*	HTx
2	16	64.9	1.70	DCM in Carvajal Syndrome	15.0	HVAD/ BTT	Median sternotomy	Post-hospital diascharge driveline infection	HTx
3	14.3	32.0	1.13	DCM Post-myocarditis	11.0	HVAD/ BTT	Median sternotomy	Bleeding requiring surgery	HTx
4	10.7	19.0	0.83	DCM	30.0	HVAD/ BTT	Median sternotomy	Bleeding requiring surgery, infection (pneumonia)	HTx
5	14.6	47.0	1.42	DCM	31.0	HVAD/ BTC	Median sternotomy	Post-hospital diascharge driveline infection	HTx
6	14.7	73.0	1.68	DCM in Duchenne Syndrome	24.0	HVAD/ DT	Median sternotomy	*None*	HTx
7	12.4	58.8	1.64	CHD post-repair	25.0	HVAD/ BTC	Median sternotomy	Cerebral anoxic coma and	Death

								death	
8	15.9	90.0	1.93	DCM	24.0	HM3/ BTC	Bilateral - thoracotomy	Post-hospital diaschar ge driveline infection	Waiti ng list
9	13.9	41	1.37	DCM post chemothe rapy	26	HM3/ BTT	Median sternoto my	*None*	HTx
1 0	11	25	1.01	DCM geneticall y mediated	18	HM3/ BTT	Median sternoto my	Bleeding requiring surgery	HTx
1 1	10.7	60	1.66	DCM geneticall y mediated	18	HM3/ BTT	Median sternoto my	*None*	Waiti ng list

BSA: Body Surface Area; BTC: Bridge-to-candidacy; BTT: Bridge-to-transplant; CHD: Congenital Heart Disease; DCM: dilative cardiomippathy; DT: destination therapy; ESHF: End-Stage Heart Failure; HTx: Heart transplant; LVEF: Left Ventricle Ejection Fraction.

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Semplicemente al coraggio,

che come i latini insegnano

viene dal cuore.