Assisted Circulation and Total Artificial Heart

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III- FUTURE

Left Ventricular Assist Devices (LVADs):
a) Bridge-to-Myocardial Recovery
b) Destination Therapy.

The Novel-LVAD III is a small intrathoracic blood pump with Atriostomy drainage.

Novel-LVAD III stabilizes the patient to make it possible the application of combination therapies.

A Strategy to Optimize Myocardial Recovery

Five approaches behind using LVAD as a tool for Myocardial Recovery or as a Destination Therapy. [1]

1- Pump inflow

The inflow pump connection from the apex of the left ventricle (LV) is clinically used today with all the commercially available devices. Undoubtedly, the geometry of the pump's inflow connector should be reconsidered, considering that it has an 18- to 20 mm-ID and destroys the helical shape of the LV myocardium. In this case the power of contraction that the LV exerts over its major axis of rotation -from the apex to the left ventricle base- is reduced.[2]

Normally the external inspection of the heart *from the apex to the base* shows a clockwise (systole) and counterclockwise (diastole) spiral motion of the myocardium, which is responsible for the heart's rotation during the cardiac cycle-ejection (systolic period) and suction (diastolic period). [3]

The hypothesis is that any further loss of the power of contraction of the LV could be catastrophic in a patient who is under circulatory assistance with a view to myocardial recovery.

Furthermore, *total ventricular unloading* favors right ventricular dysfunction, which results chiefly from the loss of the septal component in right heart contractility and the requirement of biventricular devices.

2- Partial unloading of the left ventricle

The *total unloading* currently recommended may trigger cardiomyocyte atrophy and myocardial fibrosis.[4] Even, the blood flow through the aortic valve may be stopped. Patients with a mechanical or biologic valve in the aortic position are therefore at high risk of thrombosis. Blood stagnation in the LV outflow tract may also be the source of fatal thrombo-embolic episodes.

The *partial unloading*, employing the left atrium as the pump inflow connection (atrial prosthesis), has a great simplicity. It may be managed as follows:

1- Allowing the native heart to eject from 1.8 to 2.0 L/min.

2- Regulating the LVAD output from 4.0 to 4.5 L/min

The total patient circulatory volume is 6 to 6.5 L/min.

The safe clinical method for the immediate post-surgical control should be: firstly, the total cardiac output measurement. Then, it is determined the

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[1] *Liotta D, Artificial Heart, left ventricular assist devices (LVASs): The Novel LVAS III –intrathoracic small blood puma with atriostomy drainage for combination therapies. Ann Thoracic Cardiovascular Surg, 2008, 14: 271-273 (Editorial).*

[2] *Buckberg GD, Coghlan HC, Torrent-Guasp F. The structure and function of the helical heart and its buttress wrapping. V- Anatomic and physiologic considerations in the healthy and failing heart. Semin Thoracic Cardiovasc Surg 2001; 13: 358-85.*

[3] *Torrent- Guasp F, Buckberg GD, Clemente C, Cox JL, Coghlan HC, Gharib M. The structure and function of the helical heart and its buttress wrapping. I-The normal macroscopic structure of the heart. Semin Thorac Cardiovasc Surg 2001; 13: 301-19.*

[4] *Soloff LA. Atrophy of myocardium and its myocytes by left ventricular assist device [letter]. Circulation 1999; 100: 1012.*

native LV output by regular transthoracic Doppler echocardiogram and the diastolic and systolic volumes. Further, an acceptable opening of the aortic valve must be clearly observed in each heartbeat.

At this first stage of the post-surgical period the left atrial wedge pressure, which should ideally be about 6-8 mmHg, is carefully monitored. After 2-3 days –period in which medical observations should be taken on an hourly basis-, the heart becomes adapted to the new hemodynamic situation and only periodically are echocardiography controls required.

3- ECG-synchronized LVAD employing pulsatile Systems

The ECG-synchronized LVAD offers, in theory, a better possibility of reversing profound heart failure. This chronic counterpulsation similar to the intra-aortic balloon counterpulsation increases the coronary flow. Beta-adrenergic blocking agents help to adjust the patient's heart rate to that of the pump.

Mechanical circulatory assistance improves myocardial contractile properties and increases beta-adrenergic responsiveness.[5] Although Novel LVAD can run asynchronously; in a pulsatile system, however, pump's ejection is preferable to take place in the diastolic period. [6]

4- Avoidance of left atrial and left ventricular cannulation

Cannulation of heart chambers in *LVAD-bridge-to myocardial recovery* should be avoided. It is the source of severe complications:

1- Impingement of the pump inflow connector with intraventricular structures when the LV apex is entered.

2- Left atrial collapse with an intra-atrial connector, being the source of thromboembolic complications.

5- Development of the atrial prosthesis

The key to success of LVADs is the ***atriostomy method***, which creates an opening larger than the patient's mitral valve in the lateral atrial wall.[7] A 25-mm gluteraldehyde treated biological valve is directly sutured to the left atrial wall, generally with an interrupted suture technique. Whether a continuous axial-flow device is used, only the inflow connector - instead of the valve - must be sutured to the atrial wall.

If the interrupted suture technique is used, the pledgeted sutures run from outside the atrial wall (visceral pericardium) to the endocardium, folding over the endocardium when the sutures are tied either to the valve or to the inflow connector suture ring. The pledgets remain at the atrium external surface. The 25-mm diameter atriostomy has a surface area of 4.6 square centimeters and is the elective size used in most cases of animal experiments. The 30-mm diameter has a surface area of 7 square centimeters and this is possibly the elective size in clinical use.

In calves, the atrial prosthesis may be sutured with the heart beating. In the clinical setting, the suture of the atrial prosthesis should only be done being the patient under extracorporeal circulation. The inter-atrial septum must be carefully examined, and any communication must be sutured, to prevent the risk of a right-to-left shunt.

Design of Novel LVAS -III

LVAD-III geometry of blood flow places an imaginary vault-like line from the left atrium, passing at the cardiac incisure between the lingula and the lower lobe, reaching the fifth intercostal space and continuing around the

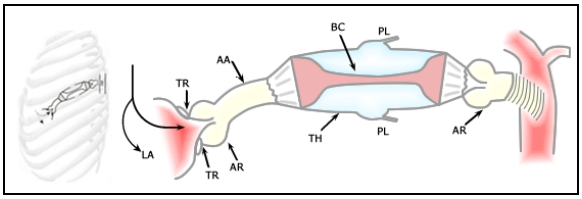
[5] *Ogletree-Hughes ML, Barrett-Stull L, Smedira NG, McCarthy PM, Moravec CS. Mechanical unloading restores beta-adrenergic responsiveness in the failing human heart [abstract]. J Heart Lung Transplant 1999;18: 63.*

[6] *Cervino C, V. Nasini, A. Sroka, A. Diluch, M. Cáceres, M. Sellanes, A. Malusardi, M. del Rio, S. Pham and D. Liotta. Novel Left Ventricular Assist Systems® I and II for Cardiac Recovery: The Driver. Tex Heart Inst J. 2005; 32(4): 535-540.*

[7] *Liotta D. Novel Left Ventricular Assist System®. An Electrocardiogram-Synchronized LVAS That Avoids Cardiac Cannulation. Tex Heart Inst J. 2003; 30(3): 194-201.*

Liotta D. Novel Left Ventricular Assist System® II. Tex Heart Inst J. 2004; 31(3): 278-282.

lower lobe to be sutured to the upper descending thoracic aorta (DTA), distally to the left subclavian artery.



Design of LVAS Novel-III

LA, left atrium; TR, titanium ring; AR, valved-aortic root (full aortic root); AsAo, ascending aorta; PH, polyurethane pump housing; BC, blood chamber; PL, pneumatic line; DTA, descending thoracic aorta.

The strategy to attempt healing the heart

First: A Novel LVAD-III with the blood path from a left atriostomy to the upper descending thoracic aorta is implanted.

Second: *LVAD serves as a Platform from which to Administer Promising Therapies.*

In selected patients the LVAD may serve as a platform for other combination therapies, for reversing the remodeling of heart failure, such as pharmacologic regimens or gene or cell-based therapies.

Research in stem cell transplantation, potential applicability in cell replacement therapies and regenerative medicine are likely to boom in the next few years and should include randomized controlled trials as well as mechanistic studies.

End Points

Primary end: Within a period from 4 to 6 months we should consider the therapeutic turnover after device insertion if gradual functional heart recovery occurred, and be prepared to electively stop mechanical circulation. The pump's body may be taken out on a later date.

Second end: There are two options for the patients that cannot be weaned off the device: a) younger patients must enter a heart transplant program; b) older patients must be considered for destination therapy.

Technical Considerations

Novel LVAD-III is implanted via a fifth intercostal space thoracotomy. In the patient placed under CPB, the aorta-mostly of the time-remains unclamped and the heart is not ischemic.

The Novel LVAD-III with blood drainage from the left atrium through an atriostomy is an ideal device as a bridge-to-myocardial recovery or as a destination therapy.

The atrial method of pump inflow can be employed today with commercially available pulsatile cardiac assistance devices (HeartMate®, Novacor®, and Thoratec®) and with continuous axial-flow devices (in-vitro studies).

In pulsatile systems, the aim of best performance of the low-frequency pump is to facilitate the synchronization of the LVAS with the patient's ECG.

A peak in blood flow and in aortic pressure during the diastolic period of the patient's cardiac cycle (chronic counterpulsation) is obtained and the integrity of the blood cells and of the pump mechanical components, including the biological valves is preserved. Furthermore, the therapy with beta-adrenergic blocking agents does not only represent a benefit for the patient but also helps adjust the natural heart frequency to that of the blood pump.

The association of beta-blockers and the diastolic ejection of the synchronized ECG- Novel LVAS may alter the global heart failure milieu.

Chronic heart failure diminishes stroke volume with chamber geometry remodeling toward a more spherical state that causes mitral regurgitation, which leads to perfusion abnormalities in systemic central organs and peripheral circulation. Indeed, mechanical chronic cardio-circulatory assist device sustenance can change the final course of the patient's illness in chronic heart failure in NYHA functional class IV.

Clearly, the bridge to heart transplantation is directed to the amelioration of the systemic circulatory milieu and not to the substantial care of heart recovery. The cardiac recovery therapy

performed by means of chronic mechanical support is related to both ameliorate the circulatory insufficiency and mainly attempt myocardial recovery.

Young[8] speculated on the causes for the low incidence of success with ventricular assist devices as a bridge-to-recovery in patients with chronic advanced heart failure. These observations indicate the importance of both surgical techniques –especially the source of blood drainage into the pump- and type of device employed for myocardial recovery.[9]

As it was mentioned above, the Novel LVAD-III also serves as a platform from which other promising therapies, such as specific pharmacologic regimens or gene or cell-based therapies may be administered to reverse heart failure. **Transplantation is not a solution to the heart failure epidemic.**

Future Directions

Left Ventricular Unloading

In the 1960s Liotta demonstrated the *functional recovery* of cardiomyocyte in cardiogenic shock postcardiotomy. His research work was confirmed through anatomical, histological and molecular biology studies in the 1990's.

Neubauer reported "*An Engine out of Fuel*" [10]; this communication contributes to open the spacious and hard path to the *myocardial recovery* project.

How will this field move forward?

Undoubtedly, larger well-controlled clinical trials must be undertaken, but at present the studies should focus on either younger patients who are scheduled to receive a heart assist device as a bridge to organ transplantation or especially non-transplant candidates, who are usually older and have more medical co-morbidites than the patients who need the device as a bridge-to-transplantation.

The trials must be powered to detect modest benefits

This is a new horizon in the surgical treatment of heart failure. It offers important changes in cellular and molecular biology where the major battles in the war against chronic failing heart will be won.

We should continue to expand cardiac surgical leadership in the development of the new molecular, cellular and clinical biology science that is certain to develop, and not to let the opportunity slip away in the exciting times to come.

The primary objective must be the regeneration of functional myocardial tissue, hence improving cardiac function for those compromised and vulnerable patients.

To summarize:

1- Pneumatic LVASs may be indicated –due to their simplicity- for short periods, 4-6 months, of cardiocirculatory assistance.

2- Further, both pulsatile and non-pulsatile Left Ventricular Assist Devices should be redesigned to be powered -every 12-24 hours- **with transcutaneous energy transfer systems.**

Left Ventricular Assist Devices must be simpler, smaller and easier to operate. These design characteristics should make these novel pumps more reliable and durable and broaden the eligible population base.

The introduction of **Non-Pulsatile flow** for Left Ventricular Assist Systems employing an **Atriostomy** for left atrial drainage has created a new physiology in the field of mechanical cardiac assistance.

Presumably, early comparative studies on clinical outcomes of Pulsatile and Non-pulsatile Left ventricular assist devices showed a functional similarity; further studies are required to support this evidence. If this were confirmed, it would indicate a more important role of Non-

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[8] *Young JB. Healing the heart with ventricular assist device therapy: mechanisms of cardiac recovery. Ann Thorac Surg 2001;71: S210-9.*

[9] *Mann DL, Willerson TJ. Left ventricular assist devices in the failing heart: a bridge-to-recovery, a permanent assist device, or a bridge too far? Circulation 1998; 98: 2367-9.*

[10] *Neubauer, S. The Failing Heart: An Engine Out of Fuel. N Eng J Med 2007;356: 1140-51.*

pulsatile LVASs in the treatment of severe heart failure.

Besides, deadly heart diseases remain among the nations´ most prominent health challenges. In fact, despite the successful approaches to prevent or limit cardiovascular disease, the severely damaged heart continues to be a formidable challenge.

Professor Alain Carpentier from the Hôpital Européen George Pompidou in Paris is conducting animal experimental trials on fully implanted artificial heart in orthotopic position. The device, which uses electronic sensors to regulate heart rate and blood flow, is incorporating new technologies on the difficult field of permanent mechanical circulation and is certainly a great medical hope in the treatment of advanced heart failure.

End of 'Assisted Circulation and Total Artificial Heart: Past, Present and Future'

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