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Brano Heart Failure Forum 2022 Conference Proceedings Paper

Highlights of the 2022 Brano Heart Failure Forum: Part Two

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Abstract

Since 2007, the Branislav “Brano” Radovancevic Heart Failure Forum (BHFF) has been held annually to provide a venue for experts to present and discuss “Innovations and New Treatment Strategies in Heart Failure.” Clinicians and researchers gather yearly in a different Eastern European city to discuss the latest in heart failure diagnostics and therapeutics. The 2022 BHFF forum was held on the 6th thru 8th of September 2022 in Trieste, Italy. It was attended by over 94 faculty from 14 countries. In addition, participation through online streaming was available. Throughout the forum, 17 sessions focused on challenges and solutions related to mechanical circulatory support (MCS) and heart transplantation. The second portion of conference highlights from available presentations is presented herein.

Left Ventricular Assist Device Complications

Perioperative Management and Neurological Complications After Left Ventricular Assist Device Implant

Presenter James Long

Despite advances in cardiac surgery in the past three decades, breakthroughs are desired in controlling adverse events, improving patients' quality of life, expanding indications, and increasing organization and cost-effectiveness.

The cumulative adverse events during the first year after surgery are significant,[1] emphasizing the importance of adverse event control. Technology has been improved; still, enhancement is needed in patient selection and management. Perioperative management can be better performed by focusing on stroke as one of the most serious adverse events.[2,3] Perioperative stroke may develop intra-operatively, so apical cannulation management should be considered to mitigate the risk.[4]

Other issues in device management include optimization of the device-host interface, thrombus formation related to cannula positioning,[5] and outflow graft handling. Both thrombi and outgraft issues are stroke risk factors for patients with a HeartMate 3 (HM3, Abbott).[6] An effort to address this issue included three-dimensional (3D) imaging and printed exoskeletons.[7]

Professional findings and debates should be widely disseminated to further advance this field. Data-driven and study-supported insights are extremely important. Similarly, outcomes of influential research bring to light issues in practice and generate useful recommended standards and guidelines.[8,9]

In conclusion, more effort must be given to optimizing and standardizing best practices, disseminating expertise field-wide, and characterizing devices.

How Can Patients with Left Ventricular Assist Device Avoid Visiting an Emergency Department?

Presenter Martin Strueber

A retrospective analysis of 44,042 records of patients with left ventricular assist devices (LVADs) who visited emergency departments from 2010 to 2017 in the United States was completed.[10] The project aimed to develop a risk model and found that the primary diagnosis on admission was an independent predictor of mortality (Table 1).[10] Importantly, stroke posed the highest mortality risk (Odds Ratio, 19.447 [95% Confidence Interval 13.1 – 28.8, P-value < .0001]).[10] Thus, cardiac-related events, gastrointestinal (GI) bleeding, and infection need to be addressed to reduce visits to the emergency room in the LVAD population.[10]

The analysis of the hospitalization patterns of LVAD recipients in the Momentum 3 trial revealed that 90% of LVAD patients were hospitalized during a two-year follow-up period; the cause of hospitalization varied, with the top diagnoses being major infection (32%), GI

bleeding (22%) and heart failure-related events (19%).[11] Recipients of the HM3 had a lower rehospitalization rate and duration than patients with a HeartMate II (Abbott); however, both groups faced the same challenges.[11] Introducing and evaluating strategies to decrease the burden of these cause-related hospitalizations is necessary to allow continuous progress in LVAD therapy. For example, GI bleeding may be better prevented if its causes are well identified, such as arteriovenous malformation during heart failure, impaired primary hemostasis, or inadequate anticoagulation.

Table 1*. Independent predictors of mortality for patients with left ventricular assist devices during an emergency department visit.*[11]

Primary Diagnosis	Odds Ratio	95% Confidence Interval
Stroke	19.4	13.1 – 28.8
Device Complication	10.1	6.5 – 16.7
Cardiac-Related	4.0	2.7 – 6.1
Infection	5.8	3.5 – 8.9
Blood Transfusion	2.6	1.8 – 4.0

In brief, recommendations for keeping LVAD patients out of the emergency room include keeping the international normalized ratio (INR) within (lower) range, changing the driveline exit side, improving mobilizations, and maximizing total cardiac output. Pulsatile and fully implantable systems are also necessary.[12]

Three-dimensional Planning for Left Ventricular Assist Devices: Chest Fitting, Least Invasive Surgical Approach, Outflow Graft Positioning

Presenter Istvan Hartyanszky

Perfect visualization is critical in cardiac surgery. 3D planning can help create optimal visualization in LVAD surgery to address the following challenges.

Inflow cannula positioning

A whole left ventricle (LV) can be reconstructed to accurately position the exoskeleton using AUTO-CAD special planning software. The proper position for the inflow cannula can be identified. A 3D-guided plastic mesh (exoskeleton) can be created, which could be used intra-operatively over the patient's heart. The conical shape of the exoskeleton and the marker line provides accurate localization on the surface of the heart.

Chest fitting

3D construction and CT scans can theoretically draw the proposed pump around the LV. The combined images would determine whether a pump would fit in a small chest.

Less invasive surgical approach and preoperative approach

Reconstructed visualization can help identify where to open the thorax. It can also be used to locate the ideal distance from the sternum and the length of the sternotomy. Such visualization can let users know if the left atrial appendage can be done from the apex or the sternotomy.

Outflow graft positioning

3D planning can help visualize the apex of the aorta. Bones and other anatomical structures can be removed to allow observation of the ascending and descending aortas.

Upgrade in the printable exoskeleton

A special plastic material is used to create the exoskeleton and internal ring. The material is soaked in a saline solution at 30°C to make the exoskeleton malleable for folding and inserting the material in small openings for minimally invasive cases.

Impact of De-Novo Aortic Regurgitation on Left Ventricular Assist Device Outcomes in 396 Patients

Presenter Hrvoje Gasparovic

The true severity of aortic regurgitation (AR) in patients with continuous-flow left ventricular assist devices (CF-LVADs) has been underestimated. De novo AR may adversely influence the performance of the device. Predictors of AR include female gender, old age, persistent valve closure, and duration of LVAD support.[13]

A cohort of 396 patients was dichotomized as without worsening AR (AR-0, 243) or with progressive AR (AR-1, 153).[14] The baseline patient characteristics were similar in both groups. The only noticeable difference was that patients with no AR progression were more likely to have HVAD placement at the time of the study.[14]

The findings were that patients experienced progressive AR over a median period of 1.4 years, and progression of AR did not lead to a reduction in survival. A 6-month follow-up showed that patients with progressive AR remained classified as New York Heart Association (NYHA) III, while patients without worsening AR were NYHA I. A difference was observed in peak O_2 uptake favoring the AR-0 group. Lower tricuspid annular plane systolic excursion values were noticed in the AR-1 group, but no difference in clinically evident right ventricular (RV) failure was found. Echocardiogram data indicated that more AR-1 patients had their aortic valves persistently closed, and patients in this group had less efficient LV unloading.

In conclusion, progressive AR is common (36%), highlighting that it is necessary to develop a revision of AR's progressive nature coupled with the duration of support and its impact on patients with mechanical circulatory devices.

New Left Ventricular Assist Devices on the Horizon

To Pulse or Not to Pulse, That Is the Question

Presenter Walter Dembitsky

Circulatory systems evolved to facilitate the transportation of nutrients and waste products over increasing distances. Research on convergent evolution has shown instances of phylogenetically unrelated species favoring the selection of pulsatile pumps for blood circulation.[15] The muscular positive-displacement pumps of the native heart offer the advantage that, under a normal state, they can generate and deliver consistent flow against dynamic and high vascular resistance while maintaining the flow pathway to minimize shear stress and stasis. The concept of biomimicry understandably inspired initial attempts to mechanically support circulation.[16,17]

Although these early pulsatile pumps were generally bio-friendly, they failed mechanically. Continuous-flow rotary pumps increased mechanical reliability and durability have favored their increasing clinical applications. However, despite significant gains in survival and quality of life, complications in patients supported by CF-LVADs have begun to appear. Gastrointestinal bleeding, aortic insufficiency, thromboembolic complications, and impaired renal function may all be the consequences of chronic exposure to the attenuated or non-pulsatile flow and high shear stress created by CF-LVADs.[18]

Fontan circulation is the longest carefully observed human experience with chronic exposure to non-pulsatile flow. It is an established strategy to treat congenital heart defect patients with a functionally univentricular heart. Acquired Fontan circuit in an adult with severe RV dysfunction is rare[19] but may evolve in chronically supported LVAD patients with RV failure. However, Fontan circulation faces adverse pulmonary vascular remodeling,[20] illustrating the principle that pulsatility in the circulation of long-term support matters. In patients with CF-LVAD support, the remodeling and fibrosis of the coronary arteries may impose physiological consequences to flow reserve, which leads to myocardial ischemia.[21] The reduction of pulsatility by a CF-LVAD induces severe periarteritis in the kidneys.[22] Carid-bulb thrombus formation is related to continuous-flow pump support.[23] Endothelial dysfunction-related neurological bleeding has also been diagnosed in patients with CF-LVADs.[24] The relationship between pulsatility and bleeding, reflected through the effect of pulsatility changes on von Willebrand factor in recipients of mechanical support devices, has also been highlighted.[25]

Therefore, pulsatility management plays an important role in the use of chronic continuous-flow mechanical support devices. The introduction of intermittent speed controls in current popular continuous-flow devices has largely served to favorably reduce stasis in the ventricle, aortic root, or the device itself. The associated flow changes could be coordinated with the pulsatile flow provided by the native heart to favor either the native heart or systemic organ recovery. Preservation of systemic pulsatility provided by the repaired native heart seems to be the best avenue to improve patient outcomes.[25] Understanding the importance of quantifying pulsatile flow as an energy gradient and not just a pressure gradient would help ensure the optimal pursuit of pulsatility in clinical practice.[26] Then, the question is not only whether to pulse or not to pulse but how much and how long.

Challenges in Heart Failure Interventions

Interatrial Shunting for Heart Failure: Concepts, Evidence, and Ongoing Studies

Presenter Sachin Kumar

Despite advances in treatment with guideline-directed medical therapy (GDMT) in the past decade, heart failure morbidity and mortality have remained high. The mortality of chronic heart failure of 10-12% at 18 months may increase to 25-40% in 5 years, depending on the patient population.[27] Elevated left atrial pressure (LAP), considered the cause of worsening symptoms, lung congestion, and hospitalization in patients with heart failure, has become a target for heart failure therapy.[28] However, LAP is difficult to manage with drug therapies alone. Newer approaches to decompress the left atrium to lower LAP have been developed.[29-31] Favorable effects of an interatrial shunt device have been shown in a preclinical proof-of-concept, chronic heart failure animal study.[29] The safety and potential effectiveness of the 5.1 mm V-Wave Ventura® Shunt Device in patients with heart failure, regardless of left ventricular ejection fraction (LVEF), was indicated in the RELIEVE-HF Roll-in Study.[30] The interatrial shunt appears to strike a good balance between left heart unloading and right heart volume handling and is a likely mechanism for RV improvement observed in the Roll-in cohort.[31] These observations need to be confirmed in the RELIEVE-HF Randomized Trial, the most important ongoing trial of interatrial shunting in heart failure, whose findings are expected to be out in late 2023.

Transcatheter Mitral Valve Implantation Before Past One's Prime: A New Cover of an Old Mechanical versus Biological Movie

Presenter Jacek Baranowski

A patient was born in 1994 and was diagnosed with dyspnea, dilated cardiomyopathy secondary to the anomalous left coronary artery from the pulmonary artery, and left coronary aorta transposition from the pulmonary artery to ascending aorta. She underwent mitral valvuloplasty with anterior papillary muscle division at 12. At 14, a Perimount Magna valve (29mm) was placed. By then, she had been through four open chest surgeries. The patient had transcatheter mitral valve implantation (TMVI) when she was 21 and gave birth to a healthy baby girl after an uneventful pregnancy at 27. She was classified as NYHA I for seven years after the delivery. However, the prognosis is not optimistic: She plans to undergo a high-risk mitral valve repair in 2030 and may need more surgeries due to endocarditis or a coronary artery bypass graft. This case raises the question of whether using a mechanical valve for this patient when she was younger was a better option.

There is no difference in long-term survival related to prosthesis type among patients 50 to 65, but a biological valve poses a higher risk of reoperation.[32] In the United States, the use of mechanical valves substantially declined among patients ≤70 years during 2008 – 2017.[33] However, mortality is lower among patients under 70 with mechanical valves when compared to patients having biological ones.[34]

Guidelines recommend that mechanical prostheses be used for patients under 65, while bio-prosthesis should be considered for patients over 65.[35,36] In patients under 70 and pregnant women, using both mechanical and biological valves poses issues with anticoagulants and absolute contraindications to non-vitamin K antagonists oral anticoagulants.[34]

Mechanical valves offer long-term benefits for patients aged 50-70 years.[37] The biological prosthesis was shown to have lower cost rates per quality-adjusted life.[38] Nevertheless, with advances in medical device industries, it may be hard to choose between mechanical and biological valves in the future.

Challenges in Heart Transplantation

Heart Transplantation for Amyloid Light Chain Amyloidosis

Presenters Concetta Di Nora, *Ugolino Livi*

Historically, systemic heart diseases have been considered a contraindication for heart transplantation.[39,40] However, patients affected by light chain cardiac amyloidosis who undergo heart transplantation followed by autologous stem cell transplantation (ASCT) have shown encouraging results.[41,42]

At Udine Hospital, 36 patients were diagnosed with systemic amyloidosis; 11/36 had cardiac failure and underwent heart transplantation. The median waitlist time was 93 days (range, 2 – 330 days). No patients died while on the waitlist. The median age at the time of diagnosis was 56 (45 – 66) years, and 67% were male. A total of eight patients underwent ASCT after heart transplantation. Peripheral blood stem cell mobilization was performed at a median of 179 days after heart transplantation, using filgrastim alone or filgrastim plus plerixafor and cyclophosphamide. ASCT was performed at a median of 277 days (184 – 473) after heart transplantation. Considering the specific characteristics of CA, we have designed a specific approach with a multidisciplinary team to monitor the status of multiorgan involvement after heart transplantation for this specific group of patients. During a median follow-up of 31 (7 – 124) months, 7 patients experienced infections, 2 had acute graft rejection of grade >2, and 1 developed skin cancer. Moreover, 1- and 5-year survival post-transplantation were 88% and 66%, respectively. Three patients had an amyloidosis relapse; one was successfully treated with the CyBorD protocol,[43] while the others died.

In conclusion, heart transplantation presents a valuable option in carefully selected patients with nearly solitary cardiac involvement. ACST after heart transplantation is an effective treatment that could decrease amyloidosis relapse and improve patients' survival.[44] Anticipated referral before end-stage cardiac or systemic involvement may be desirable at centers with experience managing this disease. After all, a multidisciplinary approach is mandatory to select patients who would benefit from this treatment.

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