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Departments

EMERGING STRATEGIES IN THE TREATMENT OF HLHS: COMBINED TRANSCATHETER & SURGICAL TECHNIQUES

By Sharon L. Hill, ACNP; Mark Galantowicz, MD and John P. Cheatham, MD

Introduction

The short and long-term outcomes for HLHS using traditional staged palliation strategies remain suboptimal. Further improvement using these traditional strategies may not be possible given the nature of the disease and the physiology established, although the Sano modification holds some promise.(1) Our "hybrid" concept of HLHS repair involves one comprehensive open heart procedure, which involves a combination of stage I, stage II, and part of stage III, flanked by two less invasive procedures to reach Fontan completion. The goal for initial stabilization is to control and protect pulmonary blood flow, provide reliable systemic cardiac output, and create unobstructed flow from the left atrium. Additionally, our goal was to develop a less invasive strategy to complete the Fontan circuit by percutaneous transcatheter therapy.

Hybrid Stage I

Between August 2001 and October 2003, 20 newborns (5 Jehovah Witness) age 1-25 days (mean 4.9 days) with weight 1.9-4.0 kg (mean 2.9 kg) underwent Hybrid Stage I palliation. All procedures were performed under general anesthesia with prostaglandin E1 infusion. We developed treatment strategies in phases based on our clinical experiences and outcomes. In phase I (n=2), the treatment was performed in the cardiac catheterization laboratory using transcatheter techniques. Two patients underwent balloon expandable PDA stent and Amplatzer® PA Flow Restrictor implantation, with conventional balloon atrial septostomy (BAS) (Figures 1A, 1B, 1C). These patients were too hemodynamically unstable with the long sheath and stiff delivery cable causing tricuspid and pulmonary valve insufficiency. In phase II (n=4), the first procedure was implantation of a balloon expandable PDA stent in the cath lab. Within 24 hours the neonate was taken to the O.R. for placement of RPA and LPA bands (PAB) performed through a median sternotomy without cardiopulmonary bypass. A 2.2 kg newborn developed unex-

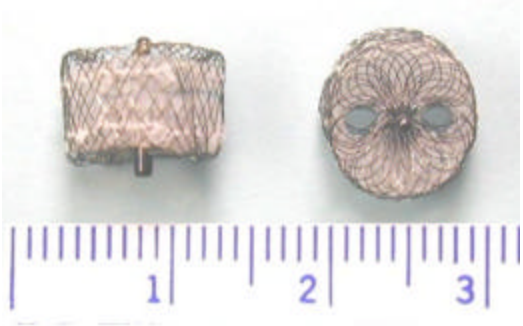

Figure 1A: The 6 mm Amplatzer® PA Flow Restrictor is shown here. Note the two 2 mm fenestrations.

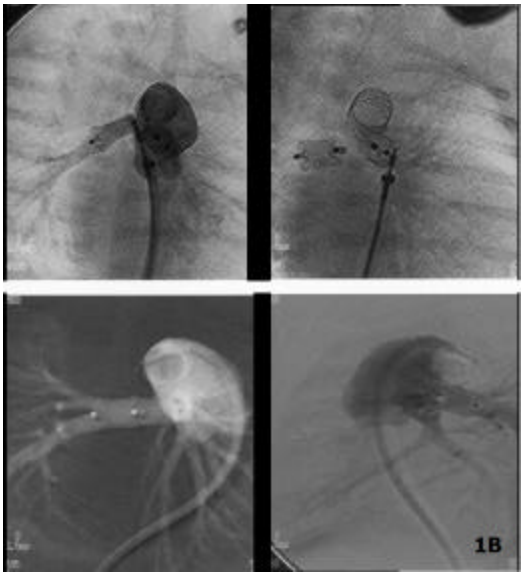

Figure 1B: This newborn had transcatheter implantation of 6 mm Flow Restrictors in the RPA & LPA. Note the balloon expandable PDA stent.

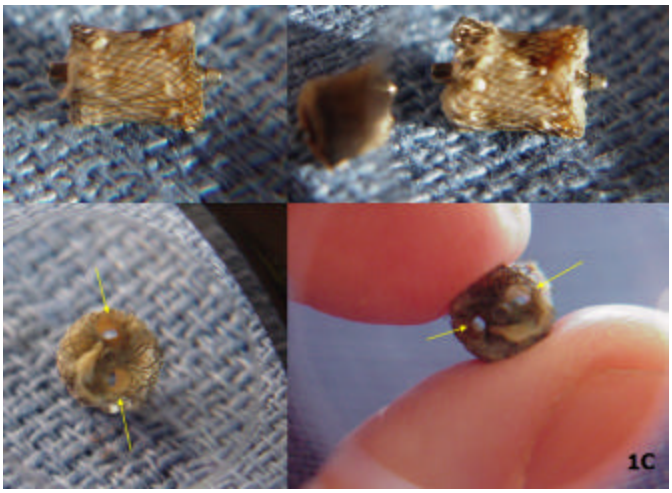

Figure 1C : After 2 ½ months the explanted PA Flow Restrictors show patent fenestrations.

plained hypotension, bradycardia, and death after BAS, awaiting PDA stent & PAB. We now perform Cutting Balloon™ and static balloon atrial septoplasty, rather than conventional BAS, to avoid trauma to the left atrium or pulmonary veins. In addition, due to the difficulty accessing the LPA with the PDA stent in place, and the symptoms of increased pulmonary blood flow, the order of the procedures was reversed. In phase III (n=7), PAB were placed in the O.R. followed by self expandable PDA stent implantation in the cath lab (Figure 2). The self expandable stent avoided a long delivery sheath and required a smaller delivery system which allowed the patients to be more hemodynamically stable. However, a 1.9 kg neonate developed intractable, fatal arrhythmias after PAB, awaiting PDA stent. In phase IV (n=7), a hybrid approach was implemented in the O.R. where PAB was performed followed by introduction of a short delivery sheath directly into the MPA. The self expandable PDA stent was deployed using a mobile, digital, cardiac C-arm. Six of the seven patients were hemodynamically stable. However, a 2.2 kg premature twin had high grade AV block and ischemia leading to intractable, fatal, ventricular arrhythmias secondary to diminished retrograde aortic flow diagnosed at autopsy to be an unsuspected congenital stenosis of the aortic arch.

Close out-patient surveillance, every 1-2 weeks, is mandatory after Hybrid Stage I palliation with close monitoring for decreased right ventricular function or increased tricuspid regurgitation as an indicator of aortic obstruction. We routinely perform a surveillance cardiac cath at 6 weeks with aggressive transcatheter treatment for any hemodynamic abnormality, i.e. restrictive ASD, PDA, or aortic coarctation. The patients are tentatively scheduled for surgery at 3 months of age.

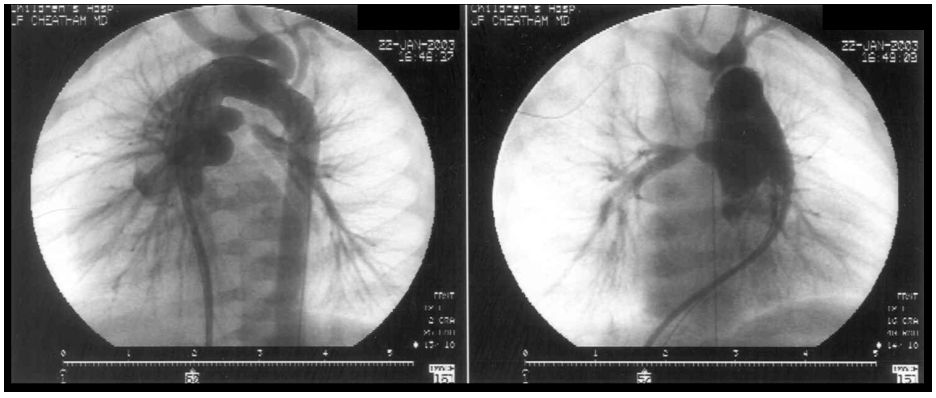

Figure 2: Tight LPA & RPA bands have been placed and represent restrictive pulmonary blood flow. In addition, relief of coarctation of the aorta is shown after successful implant of a self expandable PDA stent.

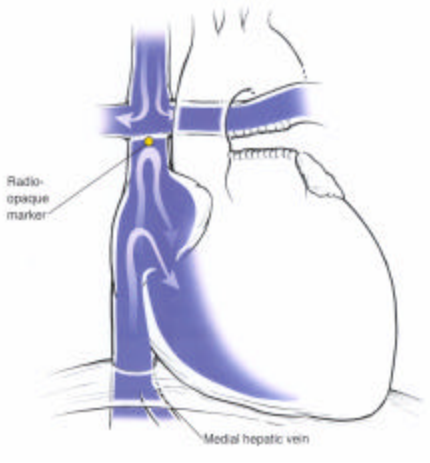

Figure 3A: Our initial modified cavopulmonary connection to facilitate transcatheter Fontan completion is depicted in this illustration.

"Comprehensive" Stage II

The "big" surgery consists of removal of the PDA stent, PA Flow Restrictors or bands, repair of the aortic arch and PA's, a DKS type PA to aorta connection, atrial septectomy, and a "modified" cavopulmonary anastomosis to facilitate transcatheter Fontan completion.(2) The goals of the surgical modification of Stage II repair are to create a blind pouch at the SVC-RA junction that could grow with the patient between procedures, serving as the anchor and marker for the subsequent transcatheter placement of a covered stent for Fontan com-

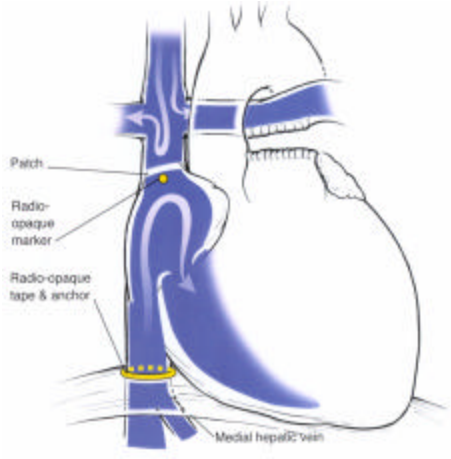

Figure 3B: The more recent modification involves oversewing the RA-SVC junction using a patch with a radio-opaque marker in the middle ("sweet spot"). A radio-opaque tape is sewn around the IVC at the level of the diaphragm to anchor the covered stent

pletion. The initial technique includes anastomosing the distal transected end of the SVC to the unopened undersurface of the PA. A radio-opaque marker was placed in the middle of the anastamosis ("sweet spot") (Figure 3A). Unfortunately, the pouch did not develop in preparation for transcatheter Fontan completion, therefore the surgical technique was revised. The newer technique involves anastamosing the transected distal end of the SVC in an open fashion to the PA, then a pericardial patch within the right atrium at the SVC-RA junction is placed to close the opening. Additionally, a strip of pericardium attached to a radio-opaque marker is placed around the IVC just distal to the IVC-RA junction to serve as an anchor for the covered stent, as well as to help identify the hepatic veins which were located below the marker (Figure 3B). Nine infants, age 2.5 – 6 months, and weight 3.8 – 5.9 kg, underwent "Comprehensive" Stage II repair. Seven patients had excellent pre-op hemodynamics, and required little inotropic support post-op, and were discharged home. Two patients had poor RV function and increased tricuspid regurgitation pre-op secondary to unrelieved aortic obstruction. Both required ECMO support post-op and subsequently expired.

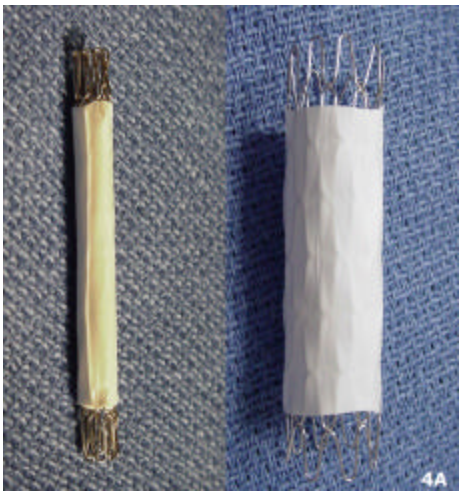

Figure 4A: This shows the e-PTFE covered NuMED CP stent before and after expansion. The leading and trailing rows of the stent are intentionally left uncovered during our initial experience.

Percutaneous Fontan Completion Stage III

From August 2001 to October 2003, 5 toddlers, mean age 23 months, and mean weight 11.3 kg, underwent percutaneous transcatheter completion of the Fontan circuit using a covered NuMED CP stent mounted on a NuMED BIB delivery catheter (Figure 4A). Using an internal jugular vein approach, transseptal needle puncture through the "sweet spot" on the floor of the PA was performed. A guidewire was advanced into the right atrium, and snared from the femoral vein to form a veno-veno "rail" system to facilitate delivery of the covered stent from below. The initial 3 patients had overlapping covered CP stents, while the latter 2 patients had a single covered stent (Figure 4B). The stents were expanded to 16-18 mm in diameter. The average oxygen saturation increased from 82 to 95%, while the average mean PA pressure increased by 1 mmHg. No blood transfusions were required and all patients were discharged home within 24 hours. Four patients returned within the first 9 months of implant with increasing cyanosis. All had variations of residual leaks at the IVC

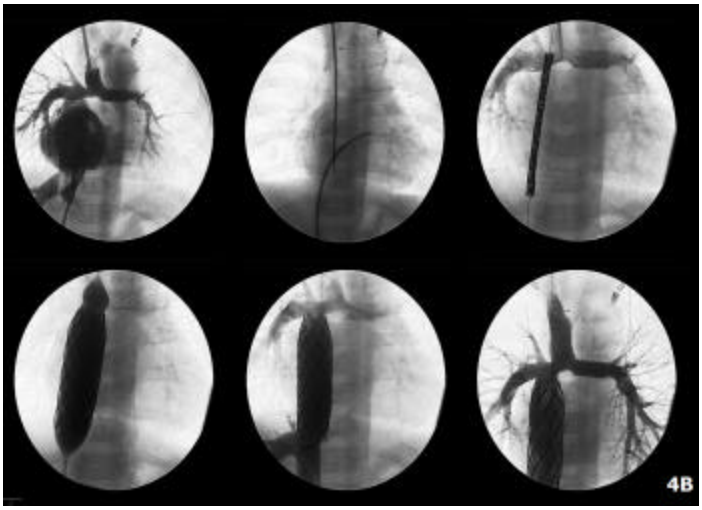

Figure 4B: This series of angiograms demonstrate the technique of transcatheter Fontan completion. After transseptal needle puncture through the "sweet spot," a veno-veno rail is established. An 8 Zig-60 mm long covered CP stent was expanded on a 16 mm BIB delivery catheter. The final angiograms demonstrate unobstructed flow from the IVC and SVC through the Fontan circuit.

end of the stent or between overlapping stents. All were successfully treated in the cath lab with additional covered stents and are currently asymptomatic and acyanotic.

Discussion

A recent report by Ashburn et al, from the CHSS registry, from 1994 to 2000 involving 29 institutions, demonstrated only a 54% survival after 5 years using conventional palliative techniques for HLHS.(3) In addition, only 46% of patients were eventual candidates for Fontan completion. Sano, et al, reported the use of an RV to PA non-valved Gore-Tex shunt instead of an aorticopulmonary shunt in these patients.(1) Their survival increased from 53% to 89% after this new modification for Stage I palliation. Michel-Behnke, et al, reported successful placement of PAB and PDA stents in 20 newborns with HLHS with only 2 procedural deaths.(4) Ten of these patients underwent successful combined Stage I and II repair at 3.5 – 6 months of age with 1 death. This report further supports our concept of the hybrid approach in the treatment of HLHS.

Future considerations include a modified approach to implant Amplatzer® PA Flow Restrictors during our Hybrid Stage I palliation in the O.R. as part of a phase I FDA sponsored clinical protocol. Modifications in stent technology, including less metal surface area, absorbable materials, and improved delivery systems may improve outcomes. Transcatheter gene therapy to maintain patency of the ductus arteriosus may be possible in the future (personal communication, Leland Benson, MD, Hospital for Sick Children, Toronto). High frequency ultrasound guided energy may be used to create atrial septal defects non-invasively, avoiding the morbidity and mortality associated with BAS in these neonates (personal communication, Achi Ludomirsky, MD, Washington University, St. Louis). Finally, the Gore Flat Ring Stent™ which allows guide wire perforation through the thin e-PTFE material may serve as an excellent anchor for the covered stent at the SVC-RA junction during transcatheter Fontan completion (personal communication, Evan Zahn, MD, Miami Children's Hospital).

"Continued collaboration between the cardiothoracic surgeon and interventional cardiologist is mandatory in order to develop innovative management strategies in the treatment of HLHS. "

Continued collaboration between the cardiothoracic surgeon and interventional cardiologist is mandatory in order to develop innovative management strategies in the treatment of HLHS. However, equally important is the support of The Heart Center personnel, including cardiologists & advanced practice nurses, cardiac anesthesia & intensive care, dedicated cardiac nursing & technical support staff.

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~PCT~

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The Heart Center at Columbus Children's Hospital, Columbus, Ohio

PROFILE: THE HEART CENTER AT COLUMBUS CHILDREN'S HOSPITAL

The Heart Center at Columbus Children's Hospital was developed to meet the comprehensive needs of an ever-growing and complex group of patients with congenital heart disease, regardless of age or severity of illness. To this end, The Heart Center has been organized into an integrated service line, both administratively and professionally, with dedicated staff to deliver the highest quality and cost effective care. The Center's faculty includes cardiologists, cardiothoracic surgeons, cardiac intensivists & anesthesiologists, dedicated cardiac advanced nurse practitioners, nurses, and allied health care professionals working seamlessly within the fifth largest Children's Hospital in the United States.

The Center's comprehensive cardiac program offers Innovative and cutting edge surgery (hybrid strategies, blood conservation, etc.) and complex transcatheter therapies (valvuloplasty, angioplasty, stents, closure devices, FDA sponsored clinical trials, etc.). A dedicated echo and cardiac imaging staff performs advanced studies (3-D TEE, ICE, fetal echocardiography, cardiac MRI, CT, etc.) and provides critical information necessary for favorable outcomes. Comprehensive clinical services are not only offered within the hospital, but also in outreach clinics throughout Central Ohio. A dedicated Adult Congenital Heart Disease Program is flourishing under the directorship of a physician, board certified in adult and pediatric cardiology, while the electrophysiology team continues to grow and offer advanced transcatheter therapies (RF ablation, 3-D mapping, PPM and ICD implants). The Heart Failure and Transplant Program was initiated in 2003 with plans to begin heart lung transplantation in the near future.

In order to expand and integrate The Heart Center services, a dedicated Telecardiology Conference Center is being constructed, which will allow connectivity to remote sites, as well as directly to the two new flat panel detector cath labs and OR suites. Finally, a state-of-the-art Hybrid Research Cardiac Cath Lab-OR Suite is to be built within the adjoining Children's Research Institute, continuing the Center's mission of developing new and innovative management strategies for the future treatment of congenital heart disease.

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Columbus, OH 43205
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~PCT~

Children's Heart Center

Selected Services

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~ Cardiac Intensive Care Specialists
~ Cardiac MRI Services
~ Cardiomyopathy & Transplantation
~ Congenital heart defects
~ Echocardiology including 3D echocardiography, fetal echocardiography
~ Electrophysiology including catheter ablation & pacemaker implantation
~ FDA research
~ Interventional cardiology
~ State-of-the-art cardiac catheterization laboratories
~ Surgery for chest wall deformities
~ Surgery for congenital heart disease

Children's HEART CENTER Columbus, Ohio

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EUROECHO 7
December 3-6, 2003 - Barcelona, Spain
www.escardio.org/

Heart Failure in Young Adults and Children
December 3-6, 2003, Houston, TX
www.heartfailureinchildren.org/

Fifth International on Interventional Cardiology - Frontiers in Interventional Cardiology
December 7-9, 2003 - Tel Aviv, Israel
www.kenes.com/intercard/

NewEra Cardiac Care Conference
January 9 - 11, 2004, Dana Point, CA
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International Congress XVII - Endovascular Interventions
February 8-12 2004, Scottsdale, AZ
www.amainc.com/index.html

Joint Interventional Meeting
February 12-14, 2004, Rome, Italy
www.jim-vascular.com/

ACC '04 (Annual Scientific Session)
March 7-10, 2004, New Orleans, LA
www.acc.org/2004ann_meeting/home/home.htm

29th Annual Scientific Meeting - 2004 SIR "The World of Intervention"
March 25-30, 2004, Phoenix, AZ
www.sirweb.org/annualMeeting/annualMeetingHome.shtml

CLINICAL TRIAL ABSTRACTS (CLINICALTRIALS.GOV)

Safety and Efficacy Study of Carvedilol to Treat Children with Congestive Heart Failure

~currently recruiting patients~

Sponsored by Robert Shaddy, M.D. Principal investigator, University of Utah

Sponsor Name Pending

Purpose: To determine whether a new medicine, called carvedilol, improves symptoms and heart function in children who have congestive heart failure (diminished function of their heart muscle that pumps blood to the body). To accomplish this, we will give carvedilol to some patients who have diminished heart function and congestive heart failure and see whether symptoms and heart function are better at the end of an 8 month period in those who received carvedilol compared to the other patients who did not receive carvedilol. The study will be testing 2 different doses of carvedilol compared to no additional medicine.

Condition: Congestive Heart Failure

Treatment: Drug: carvedilol

Phase: Phase III

Study Type: Interventional

Study Design: Treatment, Randomized, Double-Blind, Placebo Control, Parallel Assignment, Safety/Efficacy Study Official Title: A multicenter, placebo-controlled, 8-month study of the effect of twice daily carvedilol in children with congestive heart failure due to systemic ventricular systolic dysfunction

Further Study Details: Overactivity of the sympathetic nervous system is thought to contribute to the pathophysiology of congestive heart failure (CHF). Blockade of the sympathetic nervous system with ß-adrenergic inhibitors could be expected to ameliorate these detrimental effects in a manner analogous to the effects of the angiotensin converting enzyme inhibitors on the overactive renin-angiotensin system. Carvedilol may be superior to pure beta-blockers in the treatment of CHF through its mechanism of action of blocking not only ß-receptors but also a-receptors, which would allow vasodilation to reduce the afterload on the failing heart. Since beta-blockers may initially produce a negative inotropic effect on the heart, long term treatment has been needed to show benefits of removal of the adrenergic stimulation. The investigators will monitor the safety and efficacy of carvedilol administration in children with chronic CHF due to systemic ventricular dysfunction.

Eligibility: Ages Eligible for Study: up to 17 Years, Male and Female are eligible for study

Inclusion and Exclusion Criteria: See ClinicalTrials.gov

Expected Total Enrollment: 150

Location and Contact Information

Jeri L. Brown, RNC, CCRC (801) 587-7753 jeri.brown@hsc.utah.edu

Locations throughout the US (AL, AZ, CA, CO, DC, FL, GA, IL, MA, MI, MO, NY, NC, OH, PA, SC, TN, TX, UT, WI)

Study chairs or principal investigators

Robert Shaddy, M.D. University of Utah

Study ID Numbers SB 105517-321
Study Start Date May 2000; Estimated Completion Date January 2005
Record last reviewed April 2003
NLM Identifier NCT00052026
ClinicalTrials.gov processed this record on 2003-11-04

A Study of the Safety and Efficacy of rhGAA in Patients with Infantile-Onset GSD-II (Pompe Disease)

~currently recruiting patients~

Sponsored by Genzyme

Purpose: Glycogen Storage Disease Type II ("GSD-II"; also known as Pompe disease) is caused by a deficiency of a critical enzyme in the body called acid alpha-glucosidase (GAA). Normally, GAA is used by the body's cells to break down glycogen (a stored form of sugar) within specialized structures called lysosomes. In patients with GSD-II, an excessive amount of glycogen accumulates and is stored in various tissues, especially heart and skeletal muscle, which prevents their normal function. This study is being conducted to evaluate the safety and effectiveness of recombinant human acid alpha-glucosidase (rhGAA) as a potential enzyme replacement therapy for GSD-II. Patients diagnosed with infantile-onset GSD-II who are greater than 6 months old, but less than or equal to 36 months old will be studied.

Condition: Glycogen Storage Disease Type II, Pompe Disease, Acid Maltase Deficiency Disease Glycogenosis 2

Treatment : Drug: recombinant human acid alpha-glucosidase (rhGAA)

Phase: Phase I, Phase II

Study Type: Interventional

Study Design: Treatment, Non-Randomized, Open Label, Uncontrolled, Single Group Assignment, Safety/Efficacy Study

Official Title: An Open-Label, Multicenter, Multinational, Study of the Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of rhGAA Treatment in Pa-

tients Greater Than 6 Months and Less Than or Equal to 36 Months Old with Infantile-Onset GSD-II

Eligibility: Ages Eligible for Study: 6 Months - 36 Months; Both male and female eligible for study

Inclusion and Exclusion Criteria: See ClinicalTrials.gov

Expected Total Enrollment: 16

Location and Contact Information

US (FL, OK, NC), France, UK

Study ID Numbers AGLU01702
Study Start Date January 2003
Record last reviewed March 2003
NLM Identifier NCT00053573
ClinicalTrials.gov processed this record on 2003-11-04

Randomized Study of Picibanil Sclerotherapy in Children With Macrocystic Lymphangioma

~currently recruiting patients~

Sponsored by FDA Office of Orphan Products Development, University of Iowa

Purpose: Determine the efficacy of picibanil sclerotherapy in children with macrocystic lymphangioma.

Condition: Lymphatic Diseases, Lymphangioma, Cardiovascular Abnormalities

Treatment: Drug: picibanil

Study Type: Interventional

Study Design: Treatment, Efficacy Study

Further Study Details: This is a randomized, multicenter study. Patients are stratified according to prior treatment (no prior treatment vs. prior surgical treatment) and geographic area. Patients are randomized to 1 of 2 treatment arms. Arm I (Immediate treatment group): Patients receive an intralesional injection of picibanil with the aid of ultrasonography, transillumination, or fluoroscopy for localization of cysts. Treatment repeats every 6-8 weeks for a total of 4 injections. Arm II (Delayed treatment group): Patients are observed for 24-26 weeks with lesion size measured every 6-8 weeks. At the conclusion of the observation period, patients receive picibanil as in arm I. Patients with life-threatening lymphangiomas receive treatment immediately as in arm I with the option of surgical rescue. Patients are followed at 6 months, 1 year, and 2 years.

Eligibility: Ages Eligible for Study: 6 Months - 18 Years, Male and Female are eligible for study

Inclusion and Exclusion Criteria: See ClinicalTrials.gov

Expected Total Enrollment: 150

Location and Contact Information

Locations throughout US (AL, CA, IA, MN, TX, VA, WI)

Study chairs or principal investigators

Richard J. Smith, Study Chair, University of Iowa

Study ID Numbers 199/15706; UIHC-FDR001774
Study Start Date April 2000
Record last reviewed February 2001
NLM Identifier NCT00010452
ClinicalTrials.gov processed this record on 2003-11-05

CLINICALTRIALS

www.ClinicalTrials.gov

Clinical Trial Abstracts has been abstracted from the ClinicalTrials.gov Database (The U.S. NIH, Dept. of Health and Human Services, through the National Library of Medicine). *See ClinicalTrials.gov for additional up-to-date detail.*

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THE COMBINATION OF GOAL DIRECTED THERAPY AND POINT-OF-CARE TESTING DIMINISHES MORTALITY AFTER CONGENITAL HEART SURGERY

By Anthony F. Rossi, MD

While mortality for children undergoing congenital heart surgery continues to diminish, it remains substantial for certain high risk operations and neonatal palliations. Surgical modifications have had significant impact on mortality, but intensivists must continue to find ways to improve outcomes in the highest risk patients. Goal directed therapy has proven to substantially reduce morbidity and mortality in other critical illnesses such as sepsis and trauma, so it seems logical to assume that goal directed therapy may improve outcomes in patients after congenital heart surgery.

In July of 2001, the i-STAT blood gas analyzer (www.istat.com) was introduced to the cardiac intensive care unit at Miami Children's Hospital. The i-STAT analyzer was chosen because of its extreme portability (it is a handheld device) and because it was the only point-of-care device FDA approved to measure whole blood lactate. We developed a treatment algorithm based on serial blood lactate levels aimed at normalizing blood lactate as expeditiously as possible. Our belief was minimizing periods of elevated blood lactate would lead to diminishing oxygen debt.

The outcomes of patients operated on from July, 2001 through September 2003 (i-STAT group) were compared to historical controls in our institution from June 1995 through June 2001 (Pre i-STAT group). There were 710 patients in the i-STAT group and 1656 patients in the Pre i-STAT group. Patients in the i-STAT group were younger (median age 166 days vs. 311 days) and smaller (5.8 kg vs. 7.9 kg) than those in the Pre i-STAT group. Also, patients in the i-STAT group had significantly longer cardiopulmonary bypass times and aortic cross clamp times than those in the Pre i-STAT group (p=0.001 for both). The RACHS-1 score (risk for congenital heart surgery (1)) did not differ between groups (Figure 1).

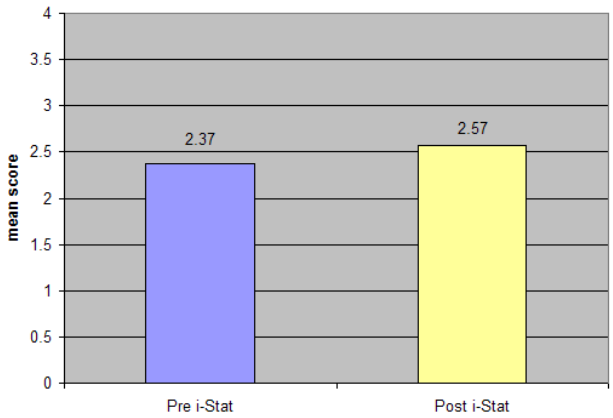

Figure 1: RASCS-1

Figures 2 and 3 demonstrate mortality as related to age for the i-STAT and Pre i-STAT groups. Figure 2 also demonstrates mortality for the 27 months immediately preceding implementation of the lactate based goal directed treatment strategy. Overall mortality was significantly lower for patients in the i-STAT group as compared to the Pre i-STAT group (1.8 % vs. 4 %, p<0.02). The patients in the i-STAT group also had a lower mortality than those operated on in the 27 months prior to i-STAT. Despite a 2/3 reduction in mortality, the difference in mortality noted in infants did not reach statistical significance. The greatest and most significant difference in mortality was noted in neonates. Patients undergoing the higher risk operations also were noted to benefit most from the goal directed therapy strategy. Patients in RACHS-1 groups 3-6 had a 66% reduction in mortality when compar-

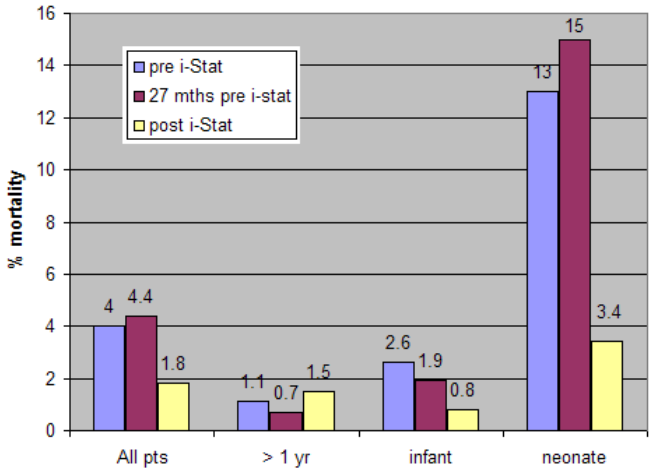

Figure 2: MCH Mortality After CHS

"Overall mortality was significantly lower for patients in the i-STAT group as compared to the Pre i-STAT group."

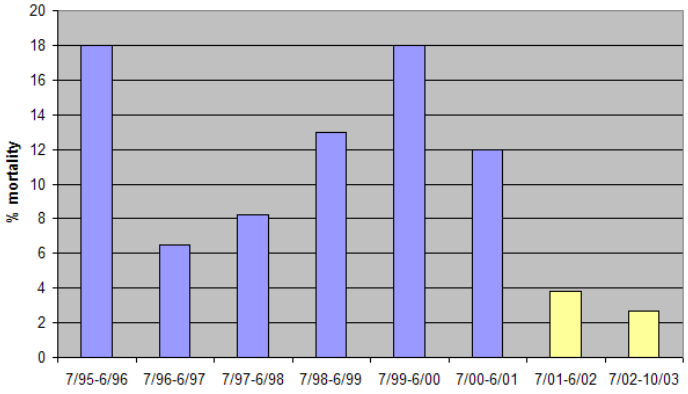

Figure 3: Neonatal Mortality by Year

ing i-STAT to Pre i-STAT eras, (3% vs. 9%, p=0.006). The greatest reduction in mortality was noted in those patients undergoing the highest risk operations, RACHS-1 5 and 6, but no difference in mortality was noted in patients undergoing lower risk operations (RACHS-1 groups 1 and 2, i-STAT 1.2% vs. Pre i-STAT 0.8%, p=NS) (Figure 4).

Lactate has proven to be an excellent predictor of morbidity and mortality in a number of critical illnesses, including children recovering from heart surgery. Some investigators have suggested that the lactate trend or duration of time where the lactate remains elevated (so called "lactime") is more important than a single lactate value in predicting mortality.(2) These investigators stress the importance of serial lactate measurements. Lactate has also proven useful as an end point of resuscitation (treatment goal) in goal directed therapy of shock. In goal directed therapy, medical management is augmented or altered until the treatment goal is reached (in this case, until lactate had normalized or begun to trend downward). In our study, we incorporated these two well established principles into the management of patients undergoing congenital heart surgery, with remarkable results. While our overall mortality was diminished by greater than 50%, it was clear that the greatest benefit of goal directed therapy occurred in both the youngest patients and in those undergoing the highest risk operations. Survival rates for patients utilizing our goal directed therapy approach have actually shown continued improvement, and the survival rate of patients undergoing surgery from January 2003 through September 2003 was greater than 99%.

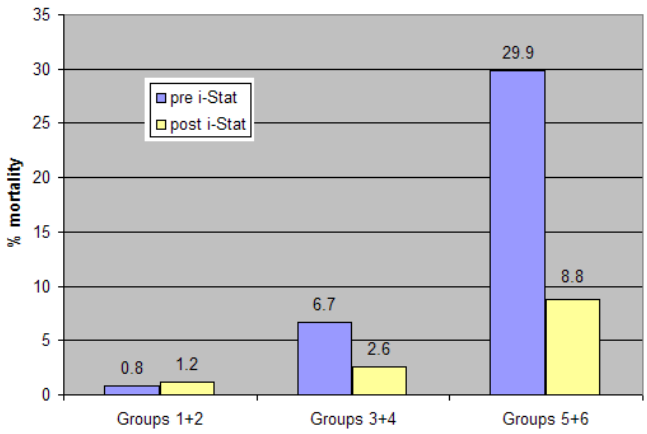

Figure 4: Mortality Related to RACHS-1 Score

Serial lactate monitoring is a simple and relatively inexpensive addition to postoperative care. With the advent of point-of-care devices such as the i-STAT blood gas analyzer, lactate can be measured with less than 30 microns of blood and a turnaround time of two minutes, giving the clinician rapid feedback during complex physiologic processes. This enables the intensivist to take prompt and appropriate action when necessary. Our results suggest that other centers should consider adapting similar treatment strategies to the routine management of patients after congenital heart surgery.

"While mortality for children undergoing congenital heart surgery continues to diminish, it remains substantial for certain high risk operations and neonatal palliations. "

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~PCT~

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IMPORTANT NEWS ABOUT DEVICE THROMBOSIS

By John W. Moore, MD, MPH

Horst Sievert's group in Frankfurt, Germany has important news from their review of one thousand patients having device closure of PFO's and ASD's in their center over a ten year period.(1) Their report is extremely important because it provides new information about device thrombosis and its consequences.

Their experience includes PFO device closures in adult patients with previous embolic events, and also a substantial number of ASD closures in younger adults and teenagers. Sievert and his colleagues implanted nine different devices, including 418 Amplatzer ASD and PFO devices, 169 CardioSEAL and StarFLEX devices, 161 Helex devices and 127 PFO-Star devices. Subsequently, they performed TEE's, in 71% of their patients, four weeks and six months after the devices were implanted.

Although transthoracic echocardiograms failed to identify patients with thrombus, they identified thrombus by TEE evaluation in 15/593 PFO patients and in 5/407 ASD patients. Thrombus was most often located in the left atrium and was usually on the device. Seventy percent (14/20) of these patients were identified at their four week TEE.

Highest on the list of factors associated with thrombus formation was type of device. 326 Amplatzer devices evaluated at four weeks were all free of thrombus. In contrast, among 119 CardioSEAL and StarFLEX devices observed at four weeks, 7 had thrombus formation (5.9%); and 5 of 76 (6.6%) PFO-Star devices examined at four weeks had thrombus. The difference between Amplatzer and these other devices was statistically significant. The Helex device was examined in 122 patients at four weeks and only one thrombus was found.

The other factors associated with thrombus formation were atrial fibrillation and persistent atrial septal aneurysm. And, the factors not associated with thrombus included coagulation disorders, coronary disease and risk factors, patient age, gender, use of protamine during the implant procedure, type of medical prophylaxis post-implant, residual shunt post-implant, and device fracture.

In patients with thrombus, Sievert and colleagues employed coumadin to dissolve the thrombus. They were successful in 85%. Three patients had surgery to remove the thrombus and perform closure of their atrial defects. Importantly, 4 of the 20 patients with thrombus suffered embolic events, including 3 minor strokes and one TIA.

"The most important observation... is that the rates of thrombosis varied significantly with device."

In their report, Sievert's group makes a number of important observations which will impact post-implant device surveillance, device selection, and perhaps also the indications for device implant.

The thrombus on the CardioSEAL, StarFLEX and PFO-Star devices justifies TEE surveillance at least at 4 weeks. However, there were no clots detected by the 4 week TEE on Amplatzer devices, and routine surveillance TEE's in patients with these devices may not be justified. The Helex and the Buttoned devices may also require less or no surveillance, but larger numbers must be studied. In addition, PFO patients with either atrial fibrillation or persistent atrial septal aneurysm, because of their greater thrombus risks, may require more surveillance than those with neither risk factor.

The most important observation by Seivert's group is that the rates of thrombosis varied significantly with device. These results are consistent with our experience at UCLA and with anecdotal reports, which document thrombosis on the PFO-Star, StarFLEX and CardioSEAL devices, but only rarely on the Amplatzer devices.(2-4) The nitinol meshwork and polyester membranes of Amplatzer devices appear to be less thrombogenic than the nitinol legs, wire superstructure, Dacron or Ivalon membranes of other devices.

Unfortunately, some issues are not resolved by the study. Sievert's group noticed a trend toward less thrombosis on the ASD devices (5/407) versus the PFO closures (15/593), which was not statistically significant. It is possible that the differing clinical characteristics of the patients, the anatomic differences between the PFOs and the ASDs, or differences in the devices used for closure, affected thrombus formation rate; but this remains speculative. Similarly, the benefit of aspirin and/or Plavix for clot prophylaxis remains uncertain.

In another recent report, King and Mills provided 27-year follow-up of the original patients in their 1976 report, which first demonstrated the feasibility of transcatheter closure of atrial septal defect (ASD).(5) Today, four of their five patients are alive and well. One patient died of old age. To the authors' knowledge, none of the patients have suffered thrombus related complications.

This 27- year anniversary offers an opportunity to take stock of where we are with transcatheter device closure of atrial shunts. The use and knowledge of ASD closure devices has grown tremendously since the King and Mills device. Modern

"...if thrombus is identified, medical treatment is usually sufficient!"

devices have minimal procedural risk, high procedural success, and as Sievert's group demonstrated in their report, a low incidence of post-implant device-related thrombus. The role of atrial devices has expanded to include closure of PFO's with the goal to prevent crytoptogenic stroke, as well as closure of hemodynamically significant ASD's. Sievert's study demonstrates that the rate of thrombosis on most commercially available devices is low enough to justify their continued use. However, the CardioSEAL, StarFLEX, and PFO Star devices require TEE surveillance in the first month after implant. Other devices, especially the Amplatzer Occluders, appear to have less risk of thrombus formation and probably do not require TEE surveillance. The good news also is that if thrombus is identified, medical treatment is usually sufficient!

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