Hope for Heart Failure

The recent addition of the 2016 AHA Guidelines, for the treatment of acute and chronic heart failure, were created to increase utilization of new treatments that complement existing therapies for all heart failure patients. These new guidelines, based upon extensive clinical research trials, have expanded treatment options for heart failure patients and improved outcomes.

Currently, six million Americans are diagnosed with heart failure. One of every five Americans will develop heart failure. Heart disease remains as the highest leading cause of death in the United States attributing to one of every four deaths in Americans with heart disease. “Heart failure is the leading cause of hospitalization in adults.” (Merck IB 21OCT 2016) Hospitalization for heart failure is associated with post-discharge mortality and readmission rates as high as 15% and 30%, respectively, within 60-90 days.

Several primary risk factors that contribute to the onset of heart failure include: coronary artery disease (heart attack), hypertension, valvular disease and diabetes. Treatment goals are to improve symptoms, prolong survival and reduce hospital readmissions. However, with current standard of care therapies, the focus on inhibiting compensatory heart failure mechanisms has proven to be less than optimal in reducing morbidity and mortality rates and fails to completely control symptoms or restore quality of life in all patients.

We are currently participating in several new heart failure clinical trials that could impact the future of heart failure therapies. These studies may include both inpatient and outpatient populations diagnosed with acute and/or chronic heart failure. Below is a brief overview of each study.

**PIONEER** “A multicenter, randomized, double-blind, double dummy, parallel group, active-controlled 8-week study to evaluate the effect of sacubitril/valsartan (LCZ696) versus enalapril on changes in NT-proBNP and safety and tolerability of in-hospital initiation of LCZ696 compared to enalapril in HFrEF patients who have been stabilized following hospitalization for acute decompensated heart failure (ADHF).” With the increased risk of mortality and rehospitalization following discharge, this study will look to introduce Entresto versus Enalapril during the acute phase of decompensated heart failure in order to improve patient outcomes.

**Dr. Wayne Gray, PI, Open to enrollment**

**Indiana University Health Ball Memorial Hospital**

**Douglas A. Triplett, MD Memorial Research Symposium**

**Friday, April 28, 2017**

**Outpatient Medical Pavilion Conference Rooms**

This year’s symposium features more than 30 projects representing works from both resident physicians and nursing personnel. The program begins at 8:00 am with a poster reception. The keynote speaker will be Sulfikar Ibrahim, MD. Dr. Ibrahim is the physician leader for the Precision Genomics Program at IU Health Ball Memorial Hospital. He obtained his undergraduate degree in Molecular Biology from the University of Maryland. He obtained his Medical Degree from the University of Maryland. He subsequently did his Residency in Internal Medicine from Drexel University and Fellowship in Hematology/ Oncology from Penn State Hershey Medical Center. He has been with IU Health Ball Memorial Hospital since 2010.
**VICTORIA**  “A Randomized Parallel-Group, Placebo-Controlled, Double-Blind, Event-Driven, Multi-Center Pivotal Phase III Clinical Outcome Trial of Efficacy and Safety of the Oral sGC Stimulator Vericiguat in Subjects With Heart Failure With Reduced Ejection Fraction (HFrEF) - VerICiguaT Global Study in Subjects With Heart Failure With Reduced Ejection Fraction (VICTORIA).” Vericiguat is a novel class of direct sGC (soluble guanylate cyclase) stimulators that target endothelial dysfunction in heart failure with the aim to reduce the cardiovascular mortality risk and heart failure rehospitalization.

*Dr. Wayne Gray, PI, Open to enrollment*

**GALACTIC**  “A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Assess the Efficacy and Safety of Omecantiv Mecarbil on Mortality and Morbidity in Subjects With Chronic Heart Failure With Reduced Ejection Fraction.” “Omecantiv mecarbil (OM) is a cardiac myosin activator that increases cardiac contractility” without the expense of increasing myocardial oxygen demands. Think of OM as a new oral therapeutic that targets myocardial contractility without the liabilities seen in traditional IV inotropes such as “no direct effect on heart rate and blood pressure, no increase in myocyte calcium, no increase in myocardial oxygen demand, or no changes in dP/dtmax.” (AMGEN Sponsor 16FEB2016)

*Dr. Wayne Gray, PI, Enrollment beginning in April 2017*

**PARADISE**  “A multi-center, randomized, double-blind, active-controlled, parallel group Phase 3 study to evaluate the efficacy and safety of LCZ696 compared to ramipril on morbidity and mortality in high risk patients following an acute myocardial infarction.” Current standard therapies recommend early initiation of ACE inhibitors after acute myocardial infarction in patients with LV systolic dysfunction alongside other evidence based pharmacotherapies. Despite these treatments, this patient population’s prognosis remains poor. Therefore, new strategies to reduce cardiovascular morbidity and mortality risks of heart failure patients are necessary. This study will evaluate “Entresto” compared to Ramipril for superiority in reducing high-risk, acute myocardial infarction heart failure morbidity and mortality incidence and improving long-term cardiovascular outcomes.

*Dr. Bruce Graham, PI, Enrollment beginning in May 2017*

**CONNECT-HF**  “Care Optimization through Patient and Hospital Engagement Clinical Trial for Heart Failure” This is a registry study to collect heart failure outcomes and quality of care after discharge from an acute heart failure hospitalization with reduced ejection fraction. It will evaluate the effectiveness of two quality improvement initiatives compared to standard of care for heart failure.

*Dr. Wayne Gray, PI, Opening summer of 2017*

**HEART-FID**  “A Randomized, Double-Blind, Placebo-Controlled study to investigate the efficacy and safety of INJECTAFER (Ferric Carboxymaltose) as therapy for patients with heart failure and iron deficiency”

*Dr. Wayne Gray, PI, Opening summer of 2017*

As one can see, there are many new and exciting possibilities for the treatment of our heart failure patients. With the new AHA heart failure guidelines and cutting edge, clinical research trials, we will hopefully see an overall improvement in heart failure morbidity/ mortality rates as well as heart failure readmission rates. More importantly, we hope to improve the quality of life for all heart failure patients. If you have a patient that might be interested in or could potentially benefit from participating in a research study, please contact the IU Health Ball Memorial Hospital Research team at 765.281.2166.

Ali Belangee, RN, BSN
Clinical Research Coordinator

Erin Loomis, RN, BSN
Clinical Research Coordinator
This original research study proposed to compare quality outcomes from two methods of blood sampling, specifically drawing blood per venipuncture and per a peripheral infusing intravenous (IV) access. The study design was correlational, and the sample was pediatric inpatients (n = 95) from IU Health Ball Memorial Hospital. The instrumentation consisted of two visual analogs scales to measure patient and family distress with the two methods of blood draws, and a single-item to assess patient/family preference for the method of blood draw. The blood test results, specifically glucose, potassium and hemoglobin, were compared across the two methods of sampling.

Key Results:
- Potassium and glucose levels were not statistically significantly different between the two blood draw methods
- Hemoglobin levels were significantly different, although the clinical significance of hemoglobin differences was negligible compared to the margin of error accepted in national laboratory guidelines
- Patient and family satisfaction was higher and patient distress was lower with the IV blood draw method (p < .001)
- Rate of hemolysis for both methods were not clinically significant, and no IVs occluded
- Presences or absence of dextrose in the IV fluid did not alter lab results
- Patients (99%) preferred the IV method
- Younger participants reported higher distress with the venipuncture method (p < .05)

Conclusions:
- Blood samples can be accurately drawn from existing infusing IVs in pediatric patients, per the study protocol for pausing the IV and flushing
- No damage to the IV site occurred from drawing blood through the IV, and no contamination of samples drawn from the IV were noted from comparison of lab results across methods
- Patients prefer the IV blood draw method, reporting higher satisfaction and less distress across all pediatric age and gender groups. Blood samples can be accurately drawn from existing infusion IVs in pediatric patients

Limitations of the Study
- Single site study with a convenience sample
- Drawing venipuncture first could increase stress, glucose and distress
- Distress ratings may have been influenced by some participants choosing to use anesthetic cream on venipuncture site
- Hemoglobin may differ slightly between blood draw methods, more so than glucose or potassium for yet unknown reasons

Future Research
- Replicate the study in ethnically diverse samples
- Conduct as a randomized control trial, with each participant assigned randomly to a blood draw group, rather than all participants experiencing both methods of blood draws
- Explore causes of slight differences in hemoglobin; test different vacutainers and check hemolysis rates

This study was funded by the Infusion Nurses Society

Renee Twibell, PhD, RN, CNE; Paula Hofstetter, BS, RN; Dava Brown, BS, RN, CRNI, VA-BC; Holly Jones, BS, RNC-OB, BC; Debra Siela, PhD, RN Indiana University Health Ball Memorial Hospital and Ball State University School of Nursing

Mona Geinosky, BSN, RN, CCRP Manager - Research

Mona Geinosky, RN Team Leader - Research
From July 1, 2016 through December 31, 2016, the following research projects and their principal investigators (PI) have been approved:

**PIONEER: CLCZ696BUS01** A multicenter, randomized, double-blind, double dummy, parallel group, active-controlled 8-week study to evaluate the effect of sacubitril and valsartan (LCZ696) versus enalapril on changes in NT-proBNP and safety and tolerability of in-hospital initiation of LCZ696 compared to enalapril in HFrEF patients who have been stabilized following hospitalization for acute decompensated heart failure (ADHF). Phase IIIb/IV

PI: Wayne Gray, MD

**NRG-BN001** Randomized Phase II Trial of Hypofractionated Dose-Escalated Photon IMRT or Proton Beam Therapy Versus Conventional Photon Irradiation With Concomitant and Adjuvant Temozolomide in Patients With Newly Diagnosed Glioblastoma

PI: Yunjie Lin, MD, PhD

**NRG-BR002** A Phase II/III Trial of Standard of Care with or without Stereotactic Body Radiotherapy (SBRT) and/or Surgical Ablation for Newly Oligometastatic Breast Cancer

PI: Yunjie Lin, MD, PhD

**Likelihood of Family Medicine and OBGYN Residents Implementing Centering Pregnancy in Future Practices**

PI: Jean Marie Place, PhD

**S1507, A Phase II Trial of Trametinib with Docetaxel in Patients with KRAS Mutation Positive Non-Small Cell Lung Cancer (NSCLC) and Progressive Disease Following One or Two Prior Systemic Therapies**

PI: Sulfikar Ibrahim, MD

**Comparison of Standardized Objective and Subjective Physical Activity Assessment for Phase II Cardiac Rehabilitation Patients**

PI: Leonard Kaminsky, PhD

**Engaging Acutely Ill Inpatients in Fall Prevention: The Effect of a Tailored Video Intervention**

PI: Renee Twibell, PhD, RN

(Victoria) A Randomized Parallel-Group, Placebo-Controlled, Double-Blind, Event-Driven, Multi-Center Pivotal Phase III Clinical Outcome Trial of Efficacy and Safety of the Oral sGC Stimulator Vericiguat in Subjects With Heart Failure With Reduced Ejection Fraction (HFrEF) - VeriCiguat Global Study in Subjects With Heart Failure With Reduced Ejection Fraction

PI: Wayne Gray, MD

**Randomized Phase II/III Trial of Prophylactic Cranial Irradiation with or without Hippocampal Avoidance for Small Cell Lung Cancer**

PI: Yunjie Lin, MD, PhD

**Collection of Specimens and Clinical Data for Precision Genomics Patients**

PI: Sulfikar Ibrahim, MD

**The effectiveness of an educational program to prevent re-admissions of heart failure patients**

PI: Leonard Kaminsky, PhD
Data Mining: Beware of Fools’ Gold

Designing clinical research is tough, and it’s natural to try and think of shortcuts to study design and data collection. Imagine this hypothetical conversation between two clinical investigators, eager to create meaningful research:

Investigator X: We need to develop a research project to get published, pronto. The deadline is approaching.

Investigator Y: I agree, X, but how will this be accomplished? Sadly, we have not invested the proper time in developing a project.

X: That’s true, Y, but we do have the database of all the clinical metrics and lab values we can use, what a shame to let that all go to waste.

Y: How so, X? Please elaborate.

X: Why, I simply set my statistical program to analyze all the different variables, and we see what is statistically significant from our huge data set, and publish those findings in the Journal.

Y: But, X, is that scientifically rigorous? We don’t even have a hypothesis for our investigation; I think I was told once we should do that first. Isn’t this doing it backwards?

X: Y, what you heard was the old way of thinking; we have computers now which are meant for analysis of large data sets. I assure you we will apply the same rigorous statistical methods as we would use with a typical study, the results will be the same.

Y: That sure makes sense to me, after explaining it that way.

Have you ever been involved in this discussion? In clinical research, it is always best to develop your hypothesis first and then collect data later. However, a practice has long existed called “data mining,” in which large data sets are examined (without an underlying hypothesis) in order to discover new connections between variables. This has developed as a research tool as computing power has increased, making the analysis of large data sets easier.

Data mining/dredging is a useful exploratory tool when large data sets exist. But this technique should, ideally, only serve as a springboard to more robust studies (those with defined, tangible hypotheses and data collection methods designed at the start), rather than trying to make a hypothesis “fit” the data (i.e., doing it “backwards.”) Engaging in this is so can lead to many problems such as false positives, false negatives, and misinterpretation due to selection bias and confounding. You should develop hypothesis before starting your study in order to prevent coming to any accidental conclusions due to data mining. Yes, it is more time-consuming to design a fresh study and collect data based on hypotheses, but this is the best way to avoid these problems.

J. Matthew Neal, MD, MBA, CPE, FACP, FACE, FAAPL
Executive Medical Director, Academic Affairs, IU Health Ball Memorial Hospital
IU Health Ball Memorial Hospital's renowned heart-care specialist Dr. Wayne L. Gray first came to Ball Memorial Hospital in 1966, as an intern. After completing his Residency and Fellowship in Cardiovascular Disease at University of Kansas Medical Center, Dr. Gray returned in 1973 to launch his career and project Ball Memorial Hospital to the cutting edge of cardiac care.

It was Dr. Gray, for example, who introduced EKG monitors and defibrillators to Ball Memorial Hospital surgery; who implemented hemodynamic monitoring in the Cardiac Intensive Care Unit; and who initiated several of the facility's acclaimed programs: Angioplasty, Two-Dimensional Echocardiography, and Cardiac Rehabilitation. While Medical Director for Quality Management, Cardiac Rehabilitation, and the Heart and Lung Center, Dr. Gray has recently been focusing closely on improving how communities at IUH BMH and beyond treat Heart Failure.

To this end, Dr. Gray is Primary Investigator for the study “Predictors of 30 day Readmission in Heart Failure Population,” and he co-wrote its protocol. “Predictors” assesses possible signs and symptoms of worsening heart failure to help determine which ones are most likely to lead to heart failure readmissions. Now closed to enrollment, the study generated complicated statistical data that has not yet been fully analyzed. Once available, this information should help our facility improve processes for treating HF to better provide individualized care, improve patients’ quality of life, and reduce readmission rates.

Concurrently, Dr. Gray is Primary Investigator for five industry studies involving acute and chronic Heart Failure, mostly concerned with treatment. Some expand indications for currently approved drugs, including a novel indication for iron infusions to improve heart function, and others introduce new classes of drugs. In conjunction with Duke University, another study centers on quality initiatives addressing heart failure outcomes.

Lately, Dr. Gray has a new project, scheduled to begin in March of this year that involves the Cardiomems implantable monitoring system developed by St. Jude Medical (they were purchased by Abbott January of 2017). The system enables outpatient hemodynamic monitoring of pulmonary pressures in heart failure patients.

Such completed, ongoing, and future investigations greatly benefit not only our patients but also our facilities. In 2011, for instance, Dr. Gray helped found IUH BMH’s Heart Failure Steering/Collaborative Committee, to begin the process of understanding total patient-care needs when facing in-patient Heart Failure; this included a Heart Failure Colloquium in 2012. As a result, the IU Health care system became the first system in the country to be nationally accredited in Heart Failure. Shortly thereafter, IU Health Ball Memorial Hospital achieved the certification.

As a member of the Heart Failure Committee, moreover, Dr. Gray championed the Heart and Lung Center that opened 1 January 2017. Its primary function is to educate and optimize treatments so that patients with chronic heart failure can prolong and enhance the quality of their lives. Located on the fourth floor of the OMP, the Center is staffed
by a Nurse Practitioner, Dreu Doerstler, and a paramedic, Scott Riffner. In addition to his other responsibilities, Scott makes house calls for patients felt to be at risk for exacerbating again. Before coming to the Heart and Lung Center, Dreu worked for ten years managing a heart-failure clinic for a group of cardiologists in Richmond. They welcomed physician referrals from the East Central Indiana Area.

Of course, Dr. Gray’s impact is not limited to the patients and facilities of IUH BMH and other IU systems. When Dr. Gray spearheaded an instructor training program and an advanced cardiac life support program for the Indiana Heart Association, for example, he helped improve all Hoosiers’ lives. While he currently serves the Nation as a fellow of the Counsel on Clinical Cardiovascular Disease with the American Heart Association, the organization expanded Dr. Gray’s reach across national boundaries, appointing him to proctor Canada’s first Advanced Cardiac Life Support program for instructors in the Cardiac Heart Association. Beyond state and national borders, moreover, Dr. Gray has published in various international publications, and was invited to the Father Muller International Cardio-Diabetes Conference in Mangalore, India, where he taught during September 2012.

Though Dr. Gray’s work has improved the lives of patients at home and abroad, those of us who have been blessed enough to work with him on a daily basis share the improved outcomes of his patients thanks to his acute wisdom, his chronically curious nature, and his unfailingly generous heart. We look forward to his continued commitment to healthy hearts everywhere for many years to come.

Sherry Adair, BS, RN, AD
Clinical Research Coordinator