

Leading the Way

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From the Chair | Douglas B. Evans, MD

Congratulations to our promoted faculty and to Drs. Christians, de Moya, Lomberk and Wang for the award of tenure. While there is a fascinating and very interesting story of the history of university tenure as well as the promotion process, both academic promotion/rank and tenure are used to reward and acknowledge academic achievement and service to the institution (to include teaching and community service as well). Indeed, they are one of several ways to appropriately recognize the contributions that everyone makes to our department and, importantly, to the care of our patients. Success in medicine is now very much team based – how to recognize, appreciate and reward the efforts of everyone on the team is both difficult and so very important. Without question, the drive home is always better when someone has complimented your work before you left. Compliments can come from anyone and mean so much. And speaking of compliments, a huge shout out to our surgical interns who now have a couple months behind them – we are so fortunate to have such a talented team of residents. Enjoy another amazing edition of “Leading the Way” – the articles cover all areas in medicine and exemplify the unique and extraordinary talent of our faculty and residents.







2022-2023 General Surgery Interns




2022 Faculty Promotions and Tenure

Congratulations to the following faculty who received a promotion or tenure effective July 1, 2022. These achievements reflect the dedication, effort, and passion of our talented faculty.





Awarded Tenure

-  Kathleen K. Christians, MD
-  Marc de Moya, MD
-  Gwen Lomberk, PhD
-  Tracy S. Wang, MD, MPH

Promoted to Professor of Surgery

-  Terri deRoos-Cassini, MS, PhD
-  David L. Joyce, MD, MBA
-  Gwen Lomberk, PhD

Promoted to Associate Professor of Surgery

-  Callisia N. Clarke, MD, MS
-  Christopher S. Davis, MD, MPH
-  Mary Elizabeth (Libby) Schroeder, MD
-  Stephanie C. Zanowski, PhD

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Profiling Surgery-Induced Immune Responses in Neuroblastoma



Brian T. Craig, MD
Assistant Professor, Pediatric Surgery

Dr. Craig was recently awarded a 2022 Jay Grosfeld, MD Scholar Grant from the American Pediatric Surgical Association Foundation to support this work, which provides \$25,000 in direct cost funding for one year for junior pediatric surgical faculty. He is also supported by a Children's Research Institute Pilot Innovation Award from Children's Wisconsin. Dr. Craig is mentored for this work by Dr. Michael Dwinell, Professor of Microbiology and Immunology, and Surgery, and Director of the Center for Immunology at MCW.

Why focus on neuroblastoma?

Children with high-risk neuroblastoma (NBL) suffer relapse rates of nearly 50% despite intensive multimodal therapy including induction chemotherapy, surgery and high-dose chemotherapy with autologous stem cell transplant. Genetic and histopathologic factors that stratify children at time of diagnosis based on overall relapse risk are well defined and determine management strategy for individual patients. However, specific drivers of relapse remain poorly understood. Surgery reduces overall tumor burden, thereby improving outcomes for children with NBL.¹ Paradoxically, evidence suggests that surgery contributes to earlier relapse across multiple cancer types, mediated by changes to antitumor immunity.² Nearly all children with high-risk NBL undergo a major operation, and are therefore exposed to the potential negative impacts of surgery.

What is the focus of the proposed study?

The overarching goal of this work is to investigate the mechanisms by which surgery may contribute to clinical relapse in NBL. Surgery initiates a shift from a cytotoxic anti-tumor lymphoid-driven immune state to a suppressive pro-tumorigenic cellular composition of macrophages, myeloid-derived suppressor cells and regulatory T cells. While these immune changes increase tumor progression and metastases in several adult cancers,³ little is known about the timing or mechanisms of acute immune changes after surgery in NBL. Our overall objective is to determine the mechanisms of immune remodeling and preclinical efficacy of immunotherapies subsequent to surgical intervention in NBL. As a critical first step, we have developed a robust preclinical model of surgery in NBL, with which we will

complete comprehensive immune profiling to define the temporal and functional outcomes of surgery on the local and systemic immune system. Our preliminary data demonstrate an increase in tumor-infiltrating T cells with a central memory phenotype in NBL tumors collected 5-7 days after surgery, suggesting that an early immune response to surgery generates a durable change in the immune system.

Investigating immune responses to surgery

The proposed study utilizes a novel surgical immune response murine model developed in our lab. Murine NBL tumor cells, derived from an oncogene-driven (MYCN) spontaneous NBL model on a C57BL/6 genetic background, are transplanted into wild-type C57BL/6 mice to generate syngeneic tumors in a host with a fully intact immune system,⁴ enabling unbiased, comprehensive immune profiling of tumor and surgery responses. Tumor-bearing mice undergo a survival abdominal laparotomy that is timed and controlled for moderate visceral tissue injury (5 minutes of intestinal exteriorization and clamp crush of the anterior liver edge) to induce a systemic inflammatory response, mimicking that which occurs after major abdominal tumor resection. The tumor remains in situ, then is harvested at an interval post-operatively and the infiltrating immune cell populations are analyzed by multiparametric flow cytometry. We anticipate this surgical immune response model will serve as a powerful discovery platform for genetic and treatment (chemotherapy, immunotherapy) interactions with both surgery and intrinsic tumor immunology.

This project has two main phases (Figure 1). The first phase of the proposed study will investigate the effects of surgery on the local and systemic immune system in NBL. We will build upon our preliminary feasibility data by systematically immune profiling peripheral blood, spleens, and tumors from animals exposed to surgery compared to non-operated tumor-bearing control mice. Immune phenotypes in neuroblastoma are only partially understood, with conflicting results reported depending on the approach used to characterize immune cell infiltration into the tumor. Our data will address this knowledge gap in the field of NBL tumor immunology, and evaluate the immune responses to surgery not just in the tumor microenvironment but also in the host macroenvironment.

In the second phase of the study, we will examine the surgery-activated chemokine networks in NBL. Chemokines direct immune cell migration by signaling through

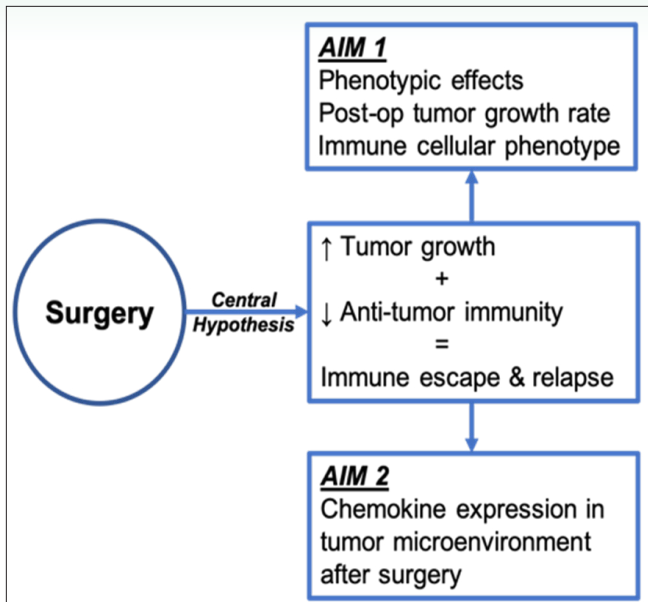


Fig 1: Schematic outline of central hypothesis and specific aims.

G protein coupled receptors in tightly regulated systems for which there are an expanding number of targeted inhibitors and antagonists currently being tested in phase I clinical trials.⁵ Activated chemokine systems can alternately promote or suppress tumor proliferation, invasion, metastasis, angiogenesis and therapy resistance either directly by acting on tumor cells or indirectly by mediating migration of immune cells. The Dwinell laboratory has demonstrated in colon and pancreas cancer that the tightly regulated chemokine networks are influenced by extrinsic stimuli and environmental cues.⁶⁻⁸ The impact of surgery on expression and function of chemokines and their G protein coupled receptors remains completely unknown. We hypothesize that chemokine ligand-receptor pairs that recruit immunosuppressive cell types such as M2-macrophages (CCR2, CCR5) and regulatory T cells (CCR4, CCR10, CXCR4) will predominate in NBL tumors, and that cytotoxic lymphocyte-related chemokine systems (e.g. CXCR3) will decrease expression after surgery exposure. We will test this hypothesis using RNA sequencing of tumors in the surgery immune response model.

Long-term vision for the project





Successful completion of the proposed work will establish the immune landscape in NBL tumors and define chemokines as a mechanism controlling immune suppression during and after surgical intervention. Chemokines and their receptors provide a therapeutically viable avenue for re-programming immune suppression and evasion after surgery. The ability to combine surgery to remove the tumor with chemokine-targeted therapies may have important clinical benefits, offering a truly novel approach to improve care for children with this devastating diagnosis.

FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Dr. Brian Craig at brcraig@chw.org.

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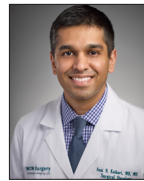
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Shifting Out of Neutral to Accelerate Clinical Insight Using Electronic Health Data



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An immense amount of data is generated with every digital interaction. From social media alone, we post 500 million tweets, send 294 billion emails, and create 4 petabytes of Facebook data—daily.¹ And as more people shift more of their lives online, the amount of data produced only increases. These data are used in many ways. For example, Apple iMessage and Google Maps use prior messages and daily commute patterns to complete text messages and predict map routes. Netflix, Hulu, and Amazon use viewing and shopping history to tailor your media and advertisement recommendations. The ease, speed, and flexibility of data activation makes this possible. And, though it can be unsettling that our data is being used in ways we do not control, these experiences with technology have become expected parts of our daily routine.

One of the largest data production industries is health care, with exabytes (1 billion gigabytes) of data produced every year from several real-world data sources, including disease registries, genomic sequencing, imaging, and digital health wearable devices.² Perhaps the largest of these is the electronic health record (EHR). Clinicians have been caught in the middle of healthcare’s digital transformation and now play a major role in data entry. A multitude of published studies have measured how EHRs have forced clinical time away from the bedside and towards a computer screen. For example, the average primary care physician is estimated to spend 5.9 out of 11.4 hours each workday on EHR documentation. A time-motion study of internal medicine residents found that approximately 112 hours per month are spent on electronic records.³

While the vast amount of potential knowledge contained within key real-world data elements—data specifically documenting and for the purpose of patient health and healthcare delivery—could support research, quality improvement, and operational priorities, these data can be seemingly impossible to retrieve. This can be explained by the complexity of data storage structures, inconsistency in data definitions, proprietary data systems, lack of interoperability, and lack of a unifying data model. As a result, the first steps to accessing these

data are often through manual chart abstraction and creating siloed datasets. Essentially, the same people that spend an enormous amount of time entering all the data into the electronic record must spend just as much (or more) time to get it back out in a usable format.

Together, these issues have led to major challenges in transforming the massive volumes of collected health-care data into something usable. The following are 5 steps (Figure 1 – 5 “gears”) that outline a roadmap to deliver data-driven insights that accelerate care improvement.

First Gear: Data Integration

Data integration refers to the consolidation of all desired data elements from multiple sources into a unifying location. Along with having an efficient method of input and output, healthcare data integration needs to be done in a manner that protects sensitive information, respects patients’ contributions, and gives credit where it’s due. A case study in data integration is the National COVID Cohort Collaborative (N3C), which provides a secure platform for accessing harmonized data from (at present) 71 unique clinical sites facilitating COVID-19 research.⁴

This data integration

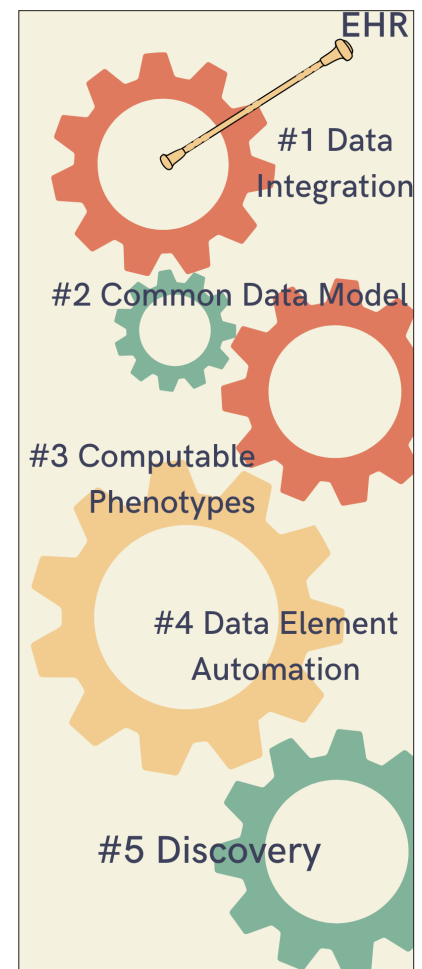


Fig 1: The five gears

has resulted in a resource that includes over 12 million patients, 680 million visits, and 14 billion unique rows of data—all readily accessible for approved investigators from across the United States.

Second Gear: Common Data Model

A common data model then facilitates the use of the integrated data. Integrating data and placing it on a single platform is analogous to bringing together a diverse group of individuals in a single room. However, if all the people spoke a different language, they would not be able to communicate effectively. Similarly, without commonalities in data language, even the most well-integrated data will not be effective. A common data model (CDM) can serve as a translator by mapping elements to shared concepts. The most widely used CDM for electronic health data is the Observational Medical Outcomes Partnership (OMOP) CDM.⁵ OMOP provides standardized healthcare terminology; it speaks a language common to several sources and sites. For example, laparoscopic cholecystectomy could be inputted as either CPT, ICD-9-CM, and/or ICD-10-PCS code. OMOP maps each of these into a single concept (laparoscopic cholecystectomy - 4163971) to ease querying and standardize abstraction.

Third Gear: Computable Phenotypes

Consolidating multiple input data types into a single, common data element gets more challenging when the concepts are more complex. A solution is the development of computable phenotypes, which are multi-step logical queries that identify clinical events or outcomes from existing data. For example, the CDC/NHSN defines superficial incisional surgical site infection (SSI) with the following set of criteria: (1) within 30 days of operative procedure AND (2) involves skin/subcutaneous tissue AND (3) has one of the following: purulent drainage OR culture identified organisms OR incision opened deliberately due to localized symptoms OR diagnosis of SSI by physician or designee. This logic could be programmed into a computable phenotype called a ‘superficial incisional surgical site infection’ using different elements within the EHR. The result is a reproducible process that extracts the data element quickly with minimal manual oversight, remains flexible to future modifications, and maps to an OMOP concept.

Fourth Gear: Data Element Automation

After leveraging the CDM and computable phenotypes, the next gear is automating extraction to provide data to the end-user. After identifying the target population, often the next step to a data-centric project is building a spreadsheet—1 row per observation with each column representing a different variable. Most of these spreadsheets have similar data element type and structure. However, there is variability on how variables are named, sourced, and defined. For effective data ele-

ment automation, the data user (who identifies the data concepts necessary for their project) and informatics team (who retrieves those data concepts and creates an automated pipeline for downstream use) require close synergy.

Fifth Gear: Discovery

Shifting into fifth gear (and beyond) is when the data is ready to be used for discovery: to support clinical trials and translational research, conduct feasibility and quality improvement studies, and research health services. Collaborative efforts have used multiple data sources and contributors, instead of one single data input, to generate highly accurate models and recognize systemic barriers to health. This includes learning from frameworks in other industries on how to utilize data most effectively. For example, the same techniques used to create email filters that analyze and flag spam could help detect inaccuracies in clinical notes. Instead of using marketing firms’ advanced analytics to target advertisements, those methodologies could facilitate personalized medicine efforts over population-level treatment recommendations.

This data science-based approach to data activation places real-world data directly in the hands of the stakeholders who can make an impact. Instead of committing resources to data abstraction and curation, energy and focus can be on data quality, efficiency, and use. Above all, it allows us to accelerate discovery.

FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Dr. Anai Kothari at akothari@mcw.edu.

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Identifying Gut Microbiome Mediated Mechanisms for Diastolic Dysfunction Improvement After Bariatric Surgery



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Gastrointestinal Surgery ; Director of Bariatric
Surgery Program, Froedtert & MCW

Heart failure with preserved ejection fraction (HFpEF) represents 50% of cases of heart failure and is closely associated with obesity.¹ Six million people in the United States have heart failure with a projected increase in prevalence of 50% by 2030.² HFpEF is a complex syndrome characterized by diastolic dysfunction, concentric left ventricular hypertrophy and high left ventricular filling pressures.³ HFpEF has significant morbidity and mortality with no effective medical treatment to decrease cardiovascular mortality.⁴ Co-morbid diseases are common in HFpEF including obesity, hypertension, type 2 diabetes mellitus, and obstructive sleep apnea.

Obesity increases circulating inflammatory mediators driving dysfunctional endothelial-cardiomyocyte signaling.⁵ Although obesity treatment would seem essential for heart failure, there are no studies demonstrating that dietary intervention with caloric restriction alone can modify cardiac function in patients with HFpEF.⁶ Contrastingly, there are multiple reports of improved cardiac function in patients with heart failure after bariatric surgery.⁷ Bariatric surgical procedures, such as a sleeve gastrectomy, produce significant and sustained weight loss. Sleeve gastrectomy, as shown in Figure 1, involves removing 75-80% of the stomach through minimally-invasive surgery. As weight loss alone is not enough to

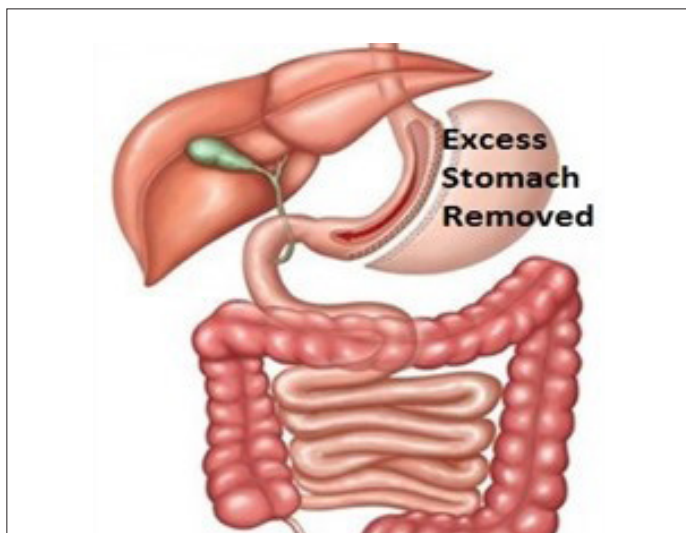


Fig 1: Sleeve gastrectomy

induce diastolic function changes, the mechanisms for cardiac recovery after bariatric surgery are unknown.

Our research laboratory at MCW was recently awarded a \$2.2 million-dollar R01 grant from the National Institutes of Health/National Heart, Lung, and Blood Institute (NIH/NHLBI) to study the mechanisms for improved diastolic dysfunction after bariatric surgery over the next five years. We hypothesize that diastolic dysfunction improves after bariatric surgery, specifically sleeve gastrectomy, due to increased bile acid signaling of the cardiac farnesoid nuclear X receptor (FXR) by altered gut microbes.

Bile acids are cholesterol metabolites that facilitate the absorption of dietary fat and fat-soluble molecules. A small fraction of the bile acid pool circulates and acts as critical metabolic regulators through activation of cellular receptors, including FXR. FXR is a ligand-activated transcription factor expressed in many tissues including cardiomyocytes.⁸ Bile acids have varying levels of FXR agonism or antagonism, with the primary bile acids, like chenodeoxycholic acid, acting as high-affinity ligands of FXR. Activation of FXR has both anti-inflammatory and antioxidant activities. Bile acid pools are depleted of FXR agonists in obesity, but significantly increased after sleeve gastrectomy, with the distinct potential to stimulate FXR and improve heart failure. In further support of the grant's hypothesis, our group has previously published that sleeve gastrectomy improves diastolic function in a weight-loss independent manner in rodents with increased cardiac FXR gene expression and decreased inflammation (Figure 2).⁹ They have also found that sleeve gastrectomy significantly increases gut microbial beta-diversity (Figure 3) including abundance of *Prevotellaceae*, a bacterium which can increase the bile acid pool and stimulate FXR.¹⁰ The grant will explore the novel mechanism that gastrointestinal anatomic changes which occur with sleeve gastrectomy, change the gut microbiota and increase *Prevotellaceae*, leading to an altered plasma bile acid pool. Increased FXR agonists within the plasma bile acid pool stimulate cardiac FXR to reduce metabolic stress and improve myocyte function.

The R01 grant has 3 main specific aims. These aims will be answered through a variety of studies which include cardiomyocyte cell cultures, rodent models of surgery, and study of human subjects undergoing sleeve gastrectomy. Aim 1 will determine whether post-sleeve gastrectomy gut microbiota increase plasma bile acid FXR agonists and improve diastolic function. This will

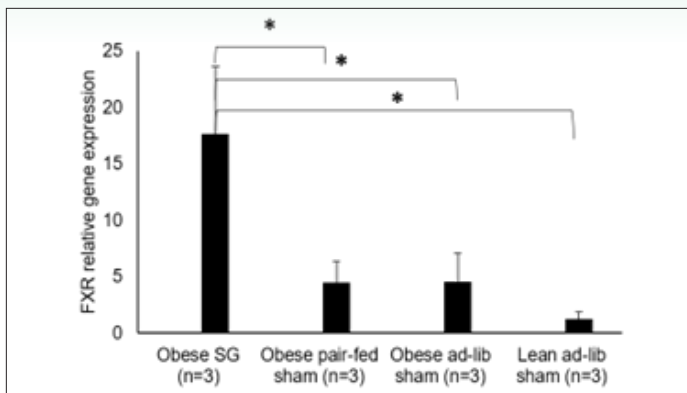


Fig 2: Sleeve gastrectomy (SG) increases cardiac FXR relative gene expression.

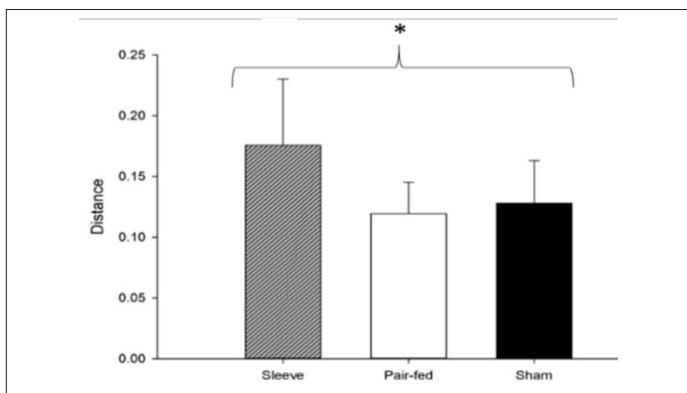


Fig 3: Sleeve gastrectomy increases beta diversity compared to pair-fed and sham obese Zucker rats. $p < 0.05$.

be tested by conducting fecal material transfer from sleeve gastrectomy mice into obese mice and measuring plasma bile acid composition and cardiac function by echocardiography. The lab will also conduct 16S and metagenomic analyses from rodents, and human stool from 24 subjects with HFpEF before and after sleeve gastrectomy, to determine bacterial metabolic functions with the potential to drive bile acid changes. This study will be done in collaboration with the MCW Bariatric Surgery Program, MCW Microbiome Research Center and University of Wisconsin Biotechnology Center. Aim 2 will determine whether sleeve gastrectomy plasma decreases cardiomyocyte metabolic stress via FXR activation. This study involves human isolated pluripotent stem cell cardiomyocytes and rodent primary cardiomyocytes which are engineered for regulated FXR expression. Blood samples are collected from rodents and human subjects (with assistance from the Clinical & Translational Science Institute Adult Translation Research Unit) after sleeve gastrectomy to determine if plasma can reduce cardiac metabolic stress through FXR agonism *in vitro*. The final aim determines whether sleeve gastrectomy improves diastolic function through cardiomyocyte FXR signaling. We will test the effect of rodent sleeve gastrectomy *in vivo* on diastolic function with regulated cardiomyocyte FXR expression.

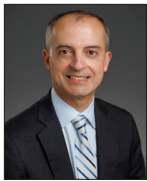
Our laboratory uses comprehensive molecular, microbial, genetic and physiological techniques in collaboration with John Kirby PhD, Chair and the Walter Schroeder Professor in Microbiology and Immunology at MCW, Michael Widlansky MD, MPH, the Northwestern Mutual Professor of Cardiovascular Medicine at MCW, and Matthew Barron PhD, Research Associate in the MCW Department of Surgery. Ultimately, our research team hopes to develop bacteria-inspired surgical and non-surgical interventions for the treatment of heart failure which replicate the metabolic mechanisms generated by sleeve gastrectomy.

FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Dr. Tammy Kindel at tkindel@mcw.edu. To learn more about the Kindel laboratory, please visit www.mcw.edu/departments/surgery/divisions/minimally-invasive-and-gastrointestinal-surgery/research/kindel-lab.

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Robotic Technology to Enhance Multidisciplinary Management of Long-Standing Atrial Fibrillation



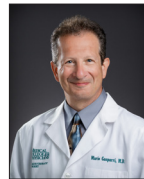
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Background

Atrial fibrillation (AF) is the most common cardiac arrhythmia with a projected prevalence of 12.1 million individuals in the US by 2030. The lifetime risk of AF has been estimated to be 1 in 3 among whites and 1 in 5 among blacks with incidence increasing with age.¹

AF is a quivering, disorganized motion of the upper heart chambers due to an unpredictable flurry of re-entrant electrical circuits. Symptoms include palpitations, chest discomfort, dyspnea and lightheadedness. AF may also lead to clot formation, particularly in the left atrial appendage (LAA) resulting in a significant risk of stroke. Long-term, AF causes considerable morbidity and mortality.² Based on the duration of such episodes, AF is classified as either “paroxysmal” (less than 7 days) or “persistent.” When AF lasts more than 12 months, it is classified as “long-standing persistent.”

Treatment strategies have varied during the past four decades ranging from medical therapy to creation of surgical “cut and sew” lesions (Cox-Maze procedure), to endocardial ablation lines using catheters with radiofrequency or cryo-energy sources.

The Cox-Maze procedure, when performed exclusively for the treatment of AF, has the highest success and stroke reduction rate regardless of AF type and remains the gold standard therapy.³ Unfortunately, its acceptance is limited due to the requirement of cardiopulmonary bypass and/or technical demands of applying the proper lesions. In an effort to achieve success similar to the Cox-Maze procedure while decreasing morbidity, hybrid approaches by

an electrophysiologist and a cardiothoracic surgeon have gained popularity.

Atrial Fibrillation and Cardiac Anatomy

Treatment of AF has evolved significantly as our understanding of how different anatomical structures contribute to the origin and propagation of these abnormal circuits has improved. Pulmonary vein (PV) isolation was the initial cornerstone,⁴ followed by improved results when ablation lines were extended to the left atrium.⁵ Full-thickness ablation of these structures allows blockade of the re-entrant circuits with significant reduction or elimination of the AF burden. While it is now understood that full-thickness ablation in key anatomic areas leads to increased success, current ablation techniques including transvenous catheter (“endocardial”) or direct external application to the heart (“epicardial”) each have their own unique limitations. When each is used exclusively, this can lead to multiple, lengthy procedures or surgical invasiveness making it less desirable to the patient. When used together, the combined epicardial

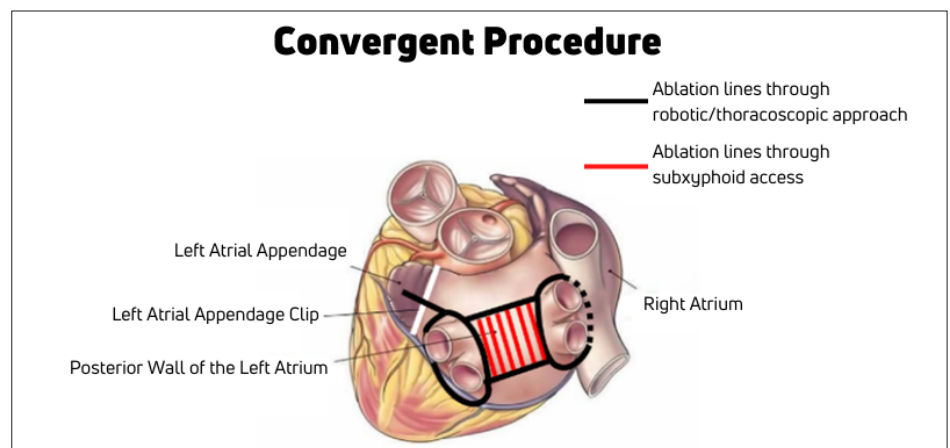


Fig. 1: Diagram representing ablation lesion sets achievable through a robotic-assisted convergent procedure.

and endocardial ablation procedure (“Convergent”), which maximizes the advantages of each approach, has shown to have increased success in treating these patients.⁶

The Hybrid Convergent Procedure (HCP)

The HCP, introduced in 2012, is a complementary treatment strategy taking advantage of the electrophysiologist’s endocardial and cardiothoracic surgeon’s epicardial approaches. In general, a surgical approach is first undertaken where the surgeon places epicardial lesions on the posterior wall of the left atrium (LA) and PV (Figure 1).⁷

The LAA is also occluded with a clip. Approximately 6-8 weeks later, the patient is returned to the EP lab where mapping and complementary ablations are performed to ensure full-thickness lesions. The hybrid approach has shown remarkable advantages including reproducing an ablation set similar to the Cox-Maze, overcoming anatomic limitations and excluding the LAA while maintaining a minimally invasive approach without the need for sternotomy and cardiopulmonary bypass. An additional advantage of the HCP is that LA posterior wall ablation can be achieved with reduced risk to the esophagus (Figure 2).

In 2020, the largest prospectively randomized trial to date (CONVERGE) reported superior effectiveness of HCP compared to catheter ablation for the treatment of patients with persistent and long-standing AF.⁸

The Froedtert and Medical College of Wisconsin Approach Through Robotic Technology

From a surgical standpoint, the initial HCP was based on a left video-assisted thoracoscopic (VATS) and sub-xiphoid approach. When we first introduced HCP at Froedtert & Medical College of Wisconsin (F&MCW) in 2017, this approach was used. Starting in 2019, in keeping with the F&MCW tradition of continuous surgical innovation, a new iteration was developed using robotic technology. Robotic surgical systems offer several advantages over VATS including 3-dimensional view and improved dexterity allowing finer dissection.⁹ With regards to the Convergent procedure, additional advantages include improved exposure to critical areas (i.e. PV, entire posterior wall of the LA, coronary sinus and LAA - Figure 3), completion of the planned lesion set in all cases, decreased perioperative complications and improved outcomes with in-hospital stay of less than 24 hours.

In addition, the robotic technology facilitates the sub-xiphoid portion of LA posterior wall ablation and allows for treatment of selected patients who underwent prior cardiac operations through sternotomy, patients in which it was previously felt this therapy could not be offered. For each patient undergoing the HCP, the LAA is also excluded through application of an appropriately sized

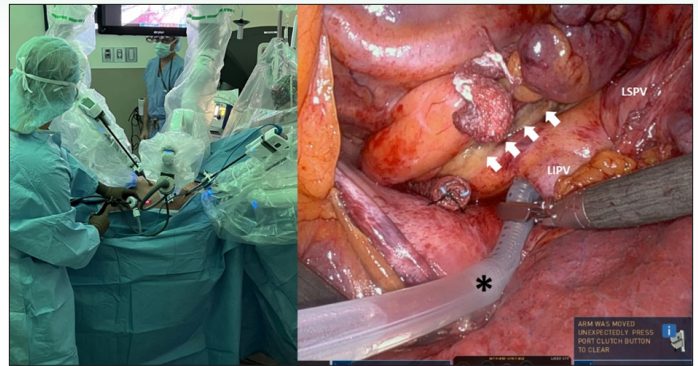


Fig. 2: Intraoperative view of the robotic system (left) and camera view (right) of a radiofrequency ablation catheter (*) applied around the pulmonary veins (LSPV= Left Superior Pulmonary Vein, LIPV= Left Inferior pulmonary vein) and recently created ablation line (arrows).

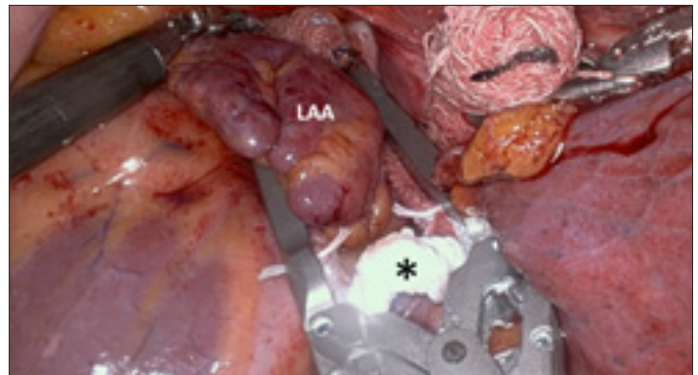


Fig. 3: Intraoperative robotic camera view of a 50 mm clip (*) applied at the base of the left atrial appendage (LAA).

clip at its base. The robotic camera allows for a more precise view of the LAA and real-time confirmation of the occluded lumen is achieved through transesophageal echocardiography.

To date, more than 40 procedures have been completed using a robotic-assisted approach at F&MCW. The median length of stay is 1 day with LAA occlusion rates of 95% and freedom from AF at 3- and 12-months follow-up of 85% and 82% respectively.

F&MCW is committed to a multidisciplinary EP/CT surgery evaluation and treatment of every patient with AF. Our collaboration ensures that each patient is evaluated thoroughly and offered a treatment plan tailored to their pathology to ensure maximal success.

FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Drs. Mario Gasparri (mgasparr@mcw.edu), Stefano Schena (sschena@mcw.edu), Marcie Berger (mgberger@mcw.edu) or James Oujiri (joujiri@mcw.edu). For clinical consultation, please contact the Division of Cardiothoracic Surgery, Froedtert Hospital & Medical College of Wisconsin at (414) 805-8296.

All Tucked in: An Improved Sleep Hygiene Protocol for Surgical Patients



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Obtaining quality sleep is a difficult challenge as a patient in the hospital. In the early hours of the morning on surgical rounds, it is common to hear multiple comments about disjointed sleep over the course of the night. Recently, there has been interest in maximizing quality of sleep while maintaining appropriate monitoring of patients during the night in the hospital. The 12CFAC accountable care team has taken this initiative to the next step, devising a new post-operative sleep hygiene protocol aimed to maximize quality sleep in eligible patients.

Poor sleep is not only a measure of poor patient satisfaction, but has also been associated with poor functional recovery, increased rates of delirium, and increased mortality.^{1,2,3} Previous studies have demonstrated that modifiable hospital-related factors affect patient sleep quality and quantity.⁴ Studies suggest that sleep disturbance may have an impact on mortality risk in the community and possibly in an inpatient setting, as well. Disjointed

or fragmented sleep, which leads to increased daytime sleeping, is associated with less functional recovery in older adults in an inpatient post-acute rehabilitation setting.¹ Patients with worse self-reported sleep quality, as



Fig 1: Door sign indicating participation in the Improved Sleep Hygiene Protocol

Inclusion Criteria

- Patients are at least POD 1 or hospital day 1
- Vital signs are stable and normal
- Urine output is: > 120 ml in 4 h or voided following operation
- Patient has ambulated following operation

Exclusion Criteria

- < 24 hours since a rapid response call
- <24 hours since transfer out of the ICU
- Free flap procedure
- Tracheostomy
- Q4 hour neuro checks
- Q4 hour vascular checks
- On a Clinical Institute Withdrawal Assessment (CIWA) protocol for alcohol
- Drains/ostomies with high output (that would require emptying during sleep time)
- Epidural catheter for pain control
- Patient controlled analgesia (PCA)/ketamine (or any other continuous intravenous pain medications requiring frequent assessment)
- Heparin or cardiac medication infusion
- Confusion/dementia, sundowning, impulsive behavior, developmental delay
- 1:1 supervision, telesitter or bed alarm
- Procedures or interventions scheduled for nighttime
- On face mask or O2 > 4L/minute on nasal cannula, high flow oxygen delivery device, or new CPAP or BiPAP

Table 1: Inclusion and Exclusion Criteria for the 12CFAC Improved Sleep Hygiene Protocol

measured by the Pittsburgh Sleep Quality Index (PSQI) had higher mortality rates.²

As an accountable care team with investment in the quality care of patients on 12CFAC, we have brainstormed what we can do on a surgical unit to maximize safe and quality sleep for our patients and promote an ideal healing environment. The proposed sleep protocol for 12CFAC will include interventions to minimize overnight interruptions and batch cares in a patient-centered model. Several studies have demonstrated the safety of implementing sleep hygiene principles on inpatient units. In a study by Patterson et al. in 2018, the safety of implementation of a multi-element sleep protocol was demonstrated.⁵ Our improved sleep hygiene protocol is based on this study, incorporating a multi-disciplinary

approach to improved sleep on a surgical unit.

The improved sleep hygiene protocol focuses on minimizing overnight interruptions by adjusting the timing of routine vitals, intake/output measurements, medication administration, and laboratory draws to give patients limited interruptions to their sleep between 0000 and 0600 hours (Table 2). Patients will have the option to be “tucked in” by their RN and CNA to promote sleep hygiene using a pre-determined checklist. Inclusion and exclusion criteria have been reviewed for patient safety (Table 1). Patients may be offered inclusion into the improved sleep hygiene protocol over the summer of 2022. The protocol will be evaluated as a quality improvement project, assessing via provider survey the impacts on sleep hygiene for included patients, rates of delirium, falls, length of stay and patient satisfaction.

Dot phrases for EPIC have been created for our physician/APP providers, a nursing communication, as well as a dot phrase for a progress note when the patient is started on the sleep protocol. A sign indicating patient participation in the sleep protocol will be posted outside the patient room (Figure 1). Provider participation in this protocol will be critical to protecting our patients’ sleep. Stay tuned for the sleep protocol implementation. We appreciate your cooperation as we work to improve the healing environment on 12CFAC.

FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Dr. Kathleen Lak at klak@mcw.edu.

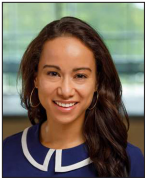
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<p>Provider</p> <ul style="list-style-type: none"> • Place Nurse Communication order to start the sleep hygiene protocol • Adjust lab order times to 0600 • Ensure VS & I & O are ordered Q8 • Review medications – <ul style="list-style-type: none"> • Eliminate unnecessary medications that would be given overnight • Enter Pharmacy Consult order to adjust medication times per the sleep protocol process • Consider ordering Melatonin for 2100, may repeat once per hour • Discuss with the patient if they are ready for the sleep protocol • Remember to not round on these patients until after 0600 in the morning • Order continuous pulse ox monitoring for sleep protocol time • Enter progress note for 12CFAC Sleep Protocol Start
<p>Pharmacist</p> <ul style="list-style-type: none"> • Adjust Q6 & Q8 hour medications to be given by 0000 and not again until 0600 • Communicate to RN &/or provider team if unable to adjust all medications • Adjust lab monitoring for therapeutic drug monitoring; communicate to team if unable to adjust lab draw time
<p>RN</p> <ul style="list-style-type: none"> • Educate patient/family on sleep protocol • Basic relaxation techniques • Offer lavender • Ensure the patient meets criteria for the sleep protocol • Limit activity and interruption in the patient rooms from 0000 – 0600 • Ensure “Tuck in Checklist” is complete
<p>CNA</p> <ul style="list-style-type: none"> • Provide HS cares by 2200 • Complete VS, blood sugar checks, & I & O by 0000 • Return for VS, blood sugar checks, & I & O at 0600 • Complete “Tuck in Checklist”

Table 2: 12CFAC Improved Sleep Hygiene Protocol Process by Role

Identifying Genetic Variants in Pursuit of Personalized Medicine for Hypoplastic Left Heart Syndrome



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Training Program



Aoy Tomita-Mitchell, PhD
Professor of Surgery and Bioengineering

Background

Hypoplastic left heart syndrome (HLHS) is a complex form of congenital heart disease (CHD) characterized by hypoplasia of the left ventricle and proximal aorta, as well as stenosis or atresia of the mitral and/or aortic valves.¹ Although significant evidence exists for a genetic basis of HLHS, its inheritance is multifactorial, complicating the identification of specific genetic risk factors. HLHS occurs in the context of larger chromosomal abnormalities (e.g., Turner and Jacobson syndromes²), but also exists as an isolated disorder.^{3,4} Additionally, there is an increased incidence of bicuspid aortic valve, atrial septal defect (ASD), and other left ventricular outflow tract (LVOT) malformations in family members of HLHS patients. Genes implicated in non-syndromic HLHS include *MYH6*⁵, *NOTCH1*, *NKX2.5*⁶, *ERBB4*, and *GJA1*.

The MCW/Herma Heart Institute (HHI) team previously identified 19 distinct, rare, predicted damaging *MYH6* variants in a cohort of 190 unrelated HLHS human subjects, comprising greater than 10% of the cohort.⁵ *MYH6* encodes for the alpha isoform of the cardiac myosin heavy chain (α -MHC). *MYH6* is expressed throughout the myocardium during early cardiac development. As development proceeds, *MYH6* expression decreases in the ventricles and is replaced with *MYH7* (β -MHC); α -MHC is the dominant atrial isoform postnatally. These findings are consistent with previous studies of zebrafish *MYH6* mutations, wherein loss-of-function mutations, gene silencing, disrupted atrial sarcomere assembly, and impaired atrial contractility resulted in atrial dilation. Mutant zebrafish embryos also exhibited ventricular wall thickening and a narrowed ventricular lumen, mimicking the HLHS phenotype. Similarly, developing *MYH6*^{-/-} *Xenopus tropicalis* hearts lacked cardiac contractility, which was accompanied by atrial and ventricular dilation and impaired outflow tract development. Although murine models are widely used to study CHD, their cardiac chamber-specific expression of MHC is opposite that of humans, making them unsuitable for modeling *MYH6*-associated disease.

Genetic variants in both *MYH6* and *MYH7* have been linked to numerous cardiac pathologies, including he-

reditary cardiomyopathies, arrhythmias, and CHD. While *MYH7* variants have been characterized extensively, the specific mechanisms underlying *MYH6* variants are less understood. A possible pathogenic role for *MYH6* was first reported more than 30 years ago in a family with hypertrophic cardiomyopathy, when investigators identified a hybrid *MYH6/MYH7* gene. Since then, additional disease-associated *MYH6* variants have been identified through family-based and CHD cohort studies. Many groups have reported *MYH6* variants in association with septal defects (most commonly ASD), as well as in various types of arrhythmias and sudden cardiac death. *MYH6* variants are also associated with all types of cardiomyopathy, and have been identified in patients with Shone complex, mitral valve prolapse, coarctation of the aorta, and HLHS.

The MCW/HHI team is investigating *MYH6* variants reported in HLHS and other CHDs to understand etiologic mechanisms and ultimately to design better, more personalized treatment strategies. The team previously identified that cardiac tissues from HLHS patients with *MYH6* variants can exhibit sarcomere disorganization in atrial but not ventricular tissues.¹⁰ The lab utilizes patient-derived induced pluripotent stem cell-derived cardiomyocytes, in combination with patient cardiac tissues, to gain mechanistic insight into how genetic variants can lead to HLHS. The study suggested that decreased contractility of CMs with a *MYH6* variant may be due to sarcomere disorganization in the atria and results in hypoplastic left ventricular development.¹⁰

Clinical Importance of Mechanistic Studies

Understanding the specific mechanism of *MYH6* variant pathogenicity would be especially relevant to clinical decision making, considering the availability of the drugs omecamtiv mecarbil and mavacamten, which act specifically on the cardiac MHCs to improve systolic and diastolic function, respectively. In phase III clinical trials, both drugs showed efficacy in the treatment of heart failure in adults,^{7,8} irrespective of genetic background; both drugs were FDA-approved earlier this year. In HLHS patients with a known pathogenic *MYH6* variant, the car-

diac specificity of omecamtiv mecarbil and mavacamten may offer a way to prevent disease progression, which is particularly important in variant carriers, given our previous report that HLHS patients with *MYH6* variants have decreased cardiac transplant-free survival compared to HLHS patients without *MYH6* variants.⁵ However, choosing to use a cardiac MHC-specific activator vs. inhibitor requires the understanding of whether a specific variant will cause systolic or diastolic dysfunction. This highlights the importance of mechanistic studies designed to understand phenotypes at the cellular and tissue levels. Relative to the large body of literature assessing *MYH7* variants, few studies have sought to understand *MYH6* variant pathology at the molecular level.

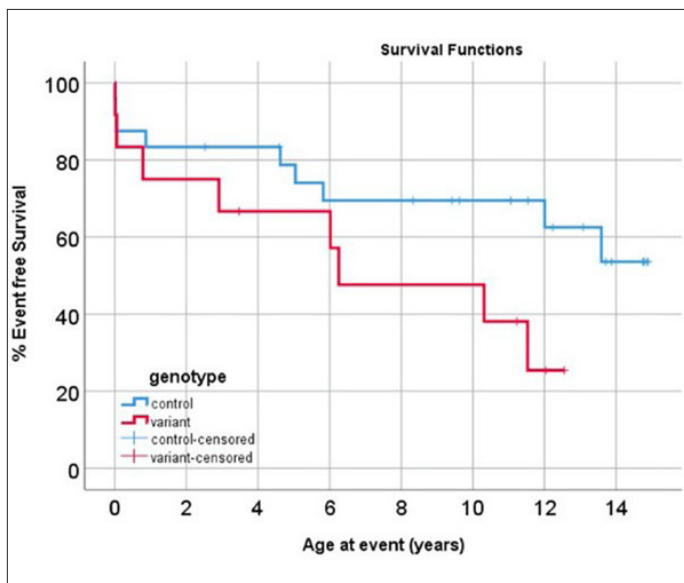


Fig. 1: Event-free survival analysis comparing 36 HLHS patients. A total of 12 patients had rare, predicting damaging *MYH6* variants. p-value = 0.074, log-rank test.

Impact of *MYH6* Variants on Outcomes in HLHS

The MCW/HHI team recently compared a composite endpoint of cardiac arrest, need for mechanical circulatory support, and heart transplant or death between 12 HLHS patients with *MYH6* variants and 24 HLHS patients without *MYH6* variants.⁹ In this cohort, each *MYH6* variant carrier was matched to two controls based on anatomical subtype (i.e., aortic and mitral valve anatomy), stage I surgical shunt type, age/era, and sex when possible. Patients with chromosomal abnormalities and those carrying *MYH7* variants were excluded. The difference in reaching the composite endpoint at 15 years between *MYH6* variant and control groups did not reach statistical significance in this small study (Figure 1), adapted from Anfinson et al.⁹ However, there is a trend towards improved short-term event-free survival in the control group.⁹ Control group outcomes appear better than previously reported transplant-free survival of HLHS patients during follow-up of the single

ventricle reconstruction (SVR) randomized trial cohort, which examined differences in transplant-free survival and interventions based on stage I surgical shunt type. These findings warrant further investigation with a larger sample size and emphasize the importance of genetic testing for all HLHS patients.

Conclusions

HLHS is a complex and genetically heterogenous disease, and the origins of HLHS are likely multigenic. Evidence suggests *MYH6* variants are etiologic in a significant percentage of HLHS. The presence of additional genetic variants and environmental influences may explain some of the clinical variability seen in presentation. In conclusion, *MYH6* variants remain an important genetic risk factor for HLHS, having prognostic significance irrespective of other factors. We anticipate that future longitudinal analyses will allow us to better understand the impact of *MYH6* variants on long-term cardiac function in HLHS which will help inform clinical decision making and highlight the importance of genetic testing.

Abridged from Anfinson et al.⁹

FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Melissa Anfinson (manfinson@mcw.edu) and Dr. Aoy Tomita-Mitchell (amitchell@mcw.edu).

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Audrey and Brenda: An Inspiring Story of Courage, Bravery, and Heroism



Johnny C. Hong, MD
Professor and Chief, Division of Transplant Surgery; Mark B. Adams Chair in Surgery



Fig 1: Audrey before her liver transplant.

Baby Audrey Huss

Audrey Huss was born full-term and immediately experienced jaundice. Bilirubin is a normal part of the pigment released from the breakdown of “used” red blood cells and is responsible for the yellow color of jaundice. Normally, the liver filters bilirubin from the bloodstream, and thus, the hyperbiliru-

binemia goes away within two weeks after birth (physiologic jaundice).

Unfortunately, Audrey’s jaundice persisted and required additional workup that led to a diagnosis of congenital biliary atresia. In this condition, there is a blockage in the ducts that carry bile from the liver to the gallbladder and intestine. The backup is caused by the absence or underdevelopment of bile ducts inside or outside the liver. With this diagnosis, Audrey underwent an operation at two months old to bypass the blocked bile duct using her small intestine, a Kasai portoenterostomy procedure. While this procedure does not cure biliary atresia, it has a reasonable chance of slowing liver damage and delaying the need for liver transplantation.

However, Audrey’s condition did not get better. Audrey’s overall health progressively declined and her jaundice worsened. She became severely malnourished and experienced refractory ascites that required paracentesis and life-threatening bleeding from poor liver function (Figure 1). What started as repeated short hospitalizations had progressed to needing aggressive medical care in the Intensive Care Unit at Children’s Wisconsin. Audrey’s liver had completely failed, and she had only a short time to live without expedited life-saving liver transplantation.

Liver Transplantation in Children: Odds Stacked Against Audrey

Organ crisis remains the principal limiting rate for the broad application of life-saving transplantation. In 2021,

among the patients on the waiting list for liver transplantation in the U.S., only 67% received transplants.¹ In addition, only 1.5% (136) were infants younger than 12 months among these liver transplant recipients. The scarcity of donated livers results in more than 2,300 patient deaths each year and is particularly devastating to small children. Children younger than two years of age carry more than a 1 in 10 risk of dying while waiting for liver transplantation compared to 1 in 20 for older children.

Furthermore, among those children who reach transplantation, more than 40% spend over a year on the waitlist, resulting in further deterioration of their medical condition. Unfortunately, there are no life-sustaining devices for end-stage liver failure patients. As a result, patients with a high acuity of illness like Audrey face imminent death without expedited liver transplantation.

Partial Liver Graft Transplantation: A Surgical Innovation in Expanding Liver Transplantation for Children

The unique ability of the liver to regenerate provided a platform for the surgical pioneers to develop innovative techniques in splitting a whole liver from a single deceased donor into two functional partial organs (grafts) and hence, saving two lives (split liver transplantation).^{2,3,4,5} The success of split liver transplantation in the 1980s paved the way for living donors to donate a part of their liver to save another life. The first successful living donor liver transplantation was performed in 1989 when a mother gave up a part of her liver to her child.⁶ With the success of adult-to-pediatric living donor liver transplantation,⁷ advances in surgical techniques allowed the safe expansion of this procedure into adult-to-adult living donor liver transplants in 1993.^{8,9} Knowledge gained in determining the appropriate liver size (functional partial organ) required to support the transplant recipient resulted in the successful utilization of partial liver grafts from living and deceased donors.¹⁰

Living Donor Liver Transplantation Program at Medical College of Wisconsin

The living donor liver transplantation program at the Medical College of Wisconsin (MCW) was started in 1999 by Dr. Mark B. Adams and inactivated in 2001. After a 12-year hiatus, Dr. Johnny C. Hong established the current living donor liver transplantation program shortly after arriving at MCW and performed the state’s first African American living donor liver transplantation

in 2013. The program received accreditation from the U.S. Department of Health and Human Services (DHSS)-Organ Procurement and Transplantation Network/United Network for Organ Sharing (OPTN/UNOS).

In 2017, Dr. Hong initiated the Anonymous (Altruistic) Living Donor Liver Transplantation Program, at a time when only 15 living donor liver transplants had been performed from anonymous living donors in the U.S. since 2013. Hence, the MCW Living Donor Liver Transplantation Program was one of few in the nation to lead this effort. In addition, the success of our anonymous living donor transplantation program gained national coverage in 2018 on ABC's "World News Tonight with David Muir." Since the inception of our living donor liver transplantation, the survival outcomes for both live donors and transplant recipients have consistently been excellent.

Anonymous Living Donor Liver Transplantation

While living donor liver donations from related family and friends have provided much-needed organs for transplantation, the gap between the demands for organs and the number of available livers remains wide. As such, liver grafts from anonymous living liver donors can increase available organs for transplantation. However, anonymous living liver donations raise ethical concerns regarding the principle of nonmaleficence. By definition, the procedure may harm the living donor for the benefit of the transplant recipient. Thus, all potential living donors must undergo a comprehensive informed consent process, particularly related to possible complications, including death and impact on the quality of life after donation. Based on national data, the complication rate with living liver donation could be up to 38%, with a death rate of 0.4%.

The Good Samaritan

Ms. Brenda Burt heard about Audrey's condition through Audrey's aunt, a coworker. While Brenda does not know Audrey, she came forward without hesitation and got tested. Even after a lengthy educational session and discussion about the risks of living liver donation, her determination to donate and save Audrey did not waver. When Dr. Hong asked her why she would do such a noble act, Brenda replied, "I am thankful to have a healthy son and would beg for someone to help my son if ever he needs [a transplant]."

Brenda underwent living donor hepatectomy (removal



Fig 2: Audrey's first birthday party with Brenda, 2 months after the transplant.

of a part of the liver) at Froedtert Hospital in December 2021. When Dr. Hong saw Brenda for the first time immediately after the operation, her first question to Dr. Hong was, "How is the baby doing?" Brenda spent the week leading up to Christmas Day in the hospital with limited visitation from her family due to the COVID-19 restricted visitor policy of the hospital. Brenda's sacrifice has been extraordinary.

A New Beginning



Fig 3: Dr. Hong and Audrey at her clinic visit 4 months after the transplant.

Audrey's recovery has been steadfast after receiving a living donor liver transplantation. Audrey celebrated her first birthday with Brenda in February 2022 (Figure 2). Moreover, she has grown substantially and is full of energy (Figure 3). As for Brenda, she recuperated well from the procedure and has resumed everyday activities. Travis and Kendra, Audrey's parents,

genuinely appreciate Brenda's heroic act and are also grateful for "the brilliant medical professionals, practices, and medicine that saved our sweet Audrey." For many of us, Brenda's act of kindness serves to restore our faith in humanity.

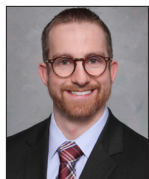
FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Dr. Johnny C. Hong at jhong@mcw.edu.

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Patient-Centered Care, Shared Decision-Making, and Thoughts on Informed Consent



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It's often that few minutes before any operation I am afforded time to reflect on the journey to where I am that day, both professionally and for the patient about to be on the table. The journey to an operating room or interventional suite is sometimes extremely short in the setting of emergency cases, and in others, years in the making. While these are very different paths, conceptually they share one great privilege – the trust a patient places in our hands to do best by him or her.

Many of us in the surgical specialties spend years, some a decade or more, understanding the art of medicine and surgery. Medicine requires dedication to life-long learning. Surgical innovation in recent decades has resulted in growing complexity in the options for treatment of nearly all disease processes. Diseases where no treatment existed now have hope; diseases where only one treatment was available now have many. The half-life of medical knowledge was estimated to be 50 years in 1950 while today it is estimated to be 18-24 months. In today's world, we have reached the point where it is difficult to keep up with emerging data in our own specialty, let alone anything outside our specialty. Despite such complexity, during this same period of time we have shifted the focus of conversation from physician-centric to a patient-centered approach to care.

In 1988, the Picker Program for Patient-Centered Care coined the term “patient-centered care.” The goal of the initiative was to shift the focus for all invested parties towards treatment options based on a patient's values.¹ The Institute of Medicine report titled “Cross-



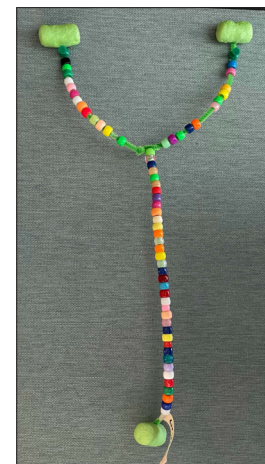
Dr. Nathan Kugler.

ing the Quality Chasm” brought it mainstream when they embodied it as a fundamental aspect of improving the quality of healthcare in the United States. Two core values are at the heart of the many different models of patient-centered care: first, a primary focus on clinician-led education of patients on treatment options, and second, active engagement of patients in

the decision-making process.

At times the above concepts seem at odds with each other. In an era where physicians outside a given specialty are often in the dark, we are tasked with educating patients on advanced treatment options in a way that he or she is actively engaged in making treatment choices. It is this fundamental process that is at the heart of informed consent – a concept not even considered law until 1914.² The term “informed consent” first appeared in court documents in 1957 in *Salgo v Leland Stanford Jr University Board of Trustees*, which created a legal obligation to provide patients with information regarding the risks, benefits, and alternatives to proposed treatment approaches.

We have made momentous strides since the days of a physician-centered approach to care to a time where patients are now empowered. The pace of surgical innovation and complexity of care begs the question of how we ensure patient-centric shared decision-making continually evolves. Explaining complex procedures, not often understood by other physicians, in a way patients understand is an incredible challenge and an art. It is those moments at the sink when we hope the patient about to be on the table truly understands the options for treatment, the risks, and benefits. Our years of training and countless informed consent discussions highlight aspects done well and certainly some not so well. Whether technical, medical, or patient interactions, we are merely a sum of those impactful moments. As we train the next generation, it is those moments shared at the scrub sink where I hope discussions with patients and efforts to embrace shared decision-making leave a positive impact on those learners. It is those moments I hope inspire them to strive to improve the quality of care we provide our patients.



Stethoscope made by Griffin Kugler, age 3.

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Takotsubo Cardiomyopathy Complicated by Arrhythmia: A Rare Presentation after Renal Transplantation

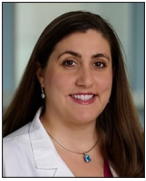
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Rising from the Ashes...Shaping the Future of Care at F&MCW



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Where we are...

As we emerge from the throes of what will likely be one of the most impactful crises of at least a few generations, there is and will continue to be a great deal of analysis, evaluation and re-evaluation, guessing and second-guessing across many industries. But health care, arguably, has been hit the hardest, positioned at ground zero in this battle between life and death. Health care workers - no matter which lane we have been swimming in or which role we have been asked, told or forced to play - are taking stock, re-examining our lives and our choices. We ask ourselves if this is still our calling, and how long we can continue to fight the good fight if this scorched and scarred landscape does not change in dramatic ways, as it never has before. We use phrases like burnt out, beaten down, spent, empty, and we look for ways to refill our cups, but relief remains scarce. Yet, as cliché or trite as it may sound, scorched earth is some of the most fertile ground, and crisis is often the best catalyst for transformative, or even disruptive, innovation.

The challenges are not unique to our organization; they plague the nation's healthcare system as a whole. We all know that the overall healthcare experience is lacking, whether we are working within it or attempting to access and find a way through it from the outside. Patients face many challenges as they navigate a clunky, poorly integrated system – lack of access, timeliness, care coordination, cost transparency, poor communication, conflicting care plans, coverage barriers, no ownership of their overall care trajectory and flow. Providers face similar challenges – process inefficiency, lack of standardization, barriers to flow of information, EMR limitations, disruptive workflows, scheduling errors, no shows, 24-7 message cycle, overflowing inboxes, excess pajama time, staffing shortages, denials, working far below license just to

get through the day.

In some ways, the challenge of the pandemic has shown us that we are capable of being adaptive and nimble, of coming together and breaking down silo walls. Yet it has also left us exposed - highlighted the gaps and emphasized the warts. Outside of our healthcare microcosm, the world has changed, too. Priorities, values, and behaviors have seemingly shifted as if overnight. The digital world leapt forward, and our patients are now not just wanting but expecting to interact with us in very different ways than ever before.



Fig. 1: Rising like a phoenix.

So, where do we go now, in healthcare and at F&MCW? Do we return to the status quo? Do we keep doing it the way we have always done it? Or do we rise like a phoenix from the ashes and take the lead in rebuilding healthcare as we and our patients want to see it, and as we all believe it could be?

I choose the phoenix (Figure 1).

Where we are going...

Over the last several months, many of you have probably seen or heard of some rather significant changes looming in the ether. Perhaps you have even heard a variety of related acronyms for different groups, committees and meetings peppered throughout daily conversa-

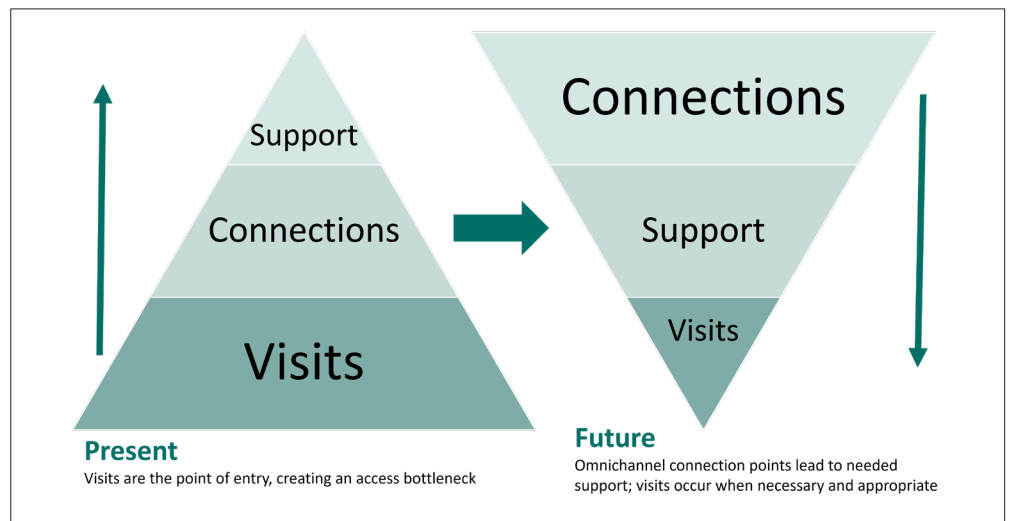


Fig. 2: A reimagination of healthcare designed around *systemness*.

tions. Among the alphabet soup, though, there is real work going on at all levels, from the front lines to the board rooms, to pivot our health system away from some of the pitfalls of the past and help us rise to meet the challenges of the post-pandemic landscape.

In FY23, F&MCW have committed to standing up a singular joint practice structure that is responsible for oversight and operations of the primary care and specialty practices both on and off campus. This initiative is designed to catalyze better alignment, enhance collaboration, create operational efficiency, generate economy of scale, and create capacity by leveraging existing resources more effectively and across a broader platform. One of the primary goals is to strengthen the provider/operator relationship and empower our front-line leaders to solve problems and remove barriers more efficiently and effectively across the practice. This work is setting the stage for the pivot toward a vision for a new care delivery model, one designed from the ground up to meet the needs of the next generation of patients and caregivers.

As the joint practice structure comes to life, F&MCW has also laid down a challenge. Front line providers and staff were selected to attend one of three visioning sessions where they were asked to think BIG, think differently, and envision anything and everything that an ideal care model of the future could be, without boundaries and free of traditional constraints. Input and feedback were collected from all areas of our organization, including primary care, specialty care, ancillary services, and support services, both on and off campus. All contributions and ideas were collated and considered throughout the process. The product of those week-long visioning sessions is both inspired and inspiring...

Imagine healthcare designed around the idea of systemness, built to facilitate at-your-fingertip connections and connectivity across all critical relationships – patients with the system, patients with caregivers, caregivers with caregivers, and caregivers with the system (Figure 2). Imagine a platform built to support maximum connectivity with our patients, providing timely answers and key touchpoints while simultaneously eliminating overflowing inboxes and provider pajama time. Imagine a system that enables real-time exchange of critical information that promotes collaboration and harmonization across a patient's entire care team while minimizing unnecessary or inappropriate questions, consults and rework. Imagine a specialty care team comprised of a wide range of highly trained skills sets that leverages each of its members at top of license so that we can meet our patients' complex needs without bottlenecking at the scarcest resource. Imagine delivering care at the nexus of technology-enabled efficiency and human knowledge, decision making and compassion.

Now, this metamorphosis will be a marathon, not a sprint. We will not see the finish line tomorrow, or even next year, and there is much work to be done to prepare for some of this transformation. It will begin with small steps and low-hanging fruit, finding ways to redeploy existing technologies and rethink existing structure and process. But the grand vision is out there, it is real, and F&MCW has committed to bringing it to life, a phoenix from the ashes. So, when you see new acronyms, or are invited to participate in new ways or on new committees, please be curious, ask questions, and lean in. It just may be your opportunity to help shape the practice of surgery as you wish to see it, and as we all wish it could be.

FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Dr. Jennifer Rabaglia at jrabaglia@mcw.edu.

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Takotsubo Cardiomyopathy Complicated by Arrhythmia: A Rare Presentation after Renal Transplantation



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Takotsubo cardiomyopathy (TTC) is an acute reversible clinical condition of unexplained origin mimicking an acute myocardial infarction (AMI). It is further recognized as broken heart syndrome or stress cardiomyopathy.

TTC has only been reported in three patients after renal and eight patients after liver transplantation.^{1,2} Of the three cases in the renal transplant population, none reported arrhythmia as a complication of TTC that required a double chamber pacemaker. We present a case of a 60-year-old woman who had renal transplantation complicated by TTC which was followed by arrhythmia.

Case report

The patient is a 60-year-old woman with a history of end-stage renal disease secondary to hypertension and diabetes; she was on dialysis for 2 years before transplant. The patient also has a history of morbid obesity, atrial fibrillation on warfarin, hypertension, and hypothyroidism. Her surgical history is significant for Gastric Bypass.

Following a successful kidney transplant, she received 1 unit of blood, 2 units of FFP, and she started to make urine immediately. The patient was transferred to recovery in stable condition. She was admitted to the Transplant Intensive Care Unit due to concern of bleeding as her procedure was performed with a therapeutic INR and she had an episode of atrial fibrillation during surgery.

Early in the morning on POD 1, the patient developed acute respiratory failure requiring emergent intubation. She also became hypotensive requiring norepinephrine and acidotic with a lactic acid of 6mmol/L. She remained awake and denied chest pain. An EKG was obtained demonstrating new left bundle branch block (LBBB) and she had mild cardiac enzymes elevation (Figure 1). The patient remained hypotensive and bradycardic, and was unresponsive to diuretics despite volume overload and hyperkalemia. Therefore, continuous renal replacement therapy (CRRT) was started.

On her echocardiogram (Figure 2), the quantitative left ventricular (LV) ejection fraction (EF) based on modi-

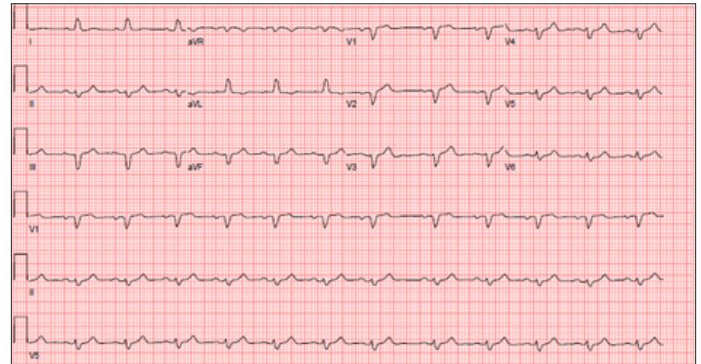


Fig 1: EKG performed when the symptoms first started. Normal sinus rhythm with sinus arrhythmia, Left axis deviation, and Left bundle branch block



Fig 2: Bedside echocardiogram consistent with Takotsubo Cardiomyopathy

fied Simpson's method was 15% with severe global hypokinesia. Due to hemodynamic compromise and new LBBB, cardiac catheterization was performed with 70% stenosis in the RCA. No intervention was required, vasopressor requirements increased and dobutamine was started.

The impact on LV function was consistent with stress-induced cardiomyopathy and cardiogenic shock. The shock team was activated, and the decision was made to place an Impella, which improved the hemodynamics significantly. She was off all vasopressors within hours

Time	LV EF (%)	Troponin T (ng/ml)
POD 1	<20%	0.054
POD 2	25-29%	1.630
POD 4	55-59%	1.070
POD 7	65-69%	0.540
POD 9	>74%	X
POD 14	>74%	X

Table 1: Post-operative trends in left ventricular ejection fraction (LVEF) and troponin T

after insertion, and it was removed after 7 days. Three days after the Impella insertion her LVEF was 54% and she was extubated (Table 1).

The patient continued to have symptomatic and frequent significant conversion pauses, multiple 6-8 second pauses, approximately one pause every minute for 15 minutes. Temporary pacing was started for treatment and when the brady-arrhythmias persisted a dual chamber pacemaker was placed.

The patient's urine output and serum creatinine improved and CRRT was discontinued. The patient eventually was discharged home after a short stay in the inpatient rehabilitation unit.

Discussion

TTC is a disease first cited by Dote and partners in 1991 at the Hiroshima City Hospital.³ The name derives from the appearance on left ventriculography at the end systolic stage, which appears shaped like a Takotsubo (bowl for trapping octopus used by Japanese fishers), due to extreme contraction of the base of the heart to compensate for extensive transient akinesia of the LV apex.

TTC has two subtypes, primary and secondary. The typical patient with primary Takotsubo syndrome is a post-menopausal woman who has encountered serious, sudden emotional or physical stress.⁴ Patients with the primary subtype present with manifestations of acute cardiac syndrome. The secondary subtype includes mainly hospitalized patients whose TTC is assumed to be precipitated by their underlying medical conditions.⁵ These changes present as an absence of obstructive coronary disease, new EKG abnormalities such as ST-segment elevation and/or T-wave inversion, or modest elevation in cardiac troponins.

A report on the prevalence of TTC by Deshmukh A et al based on nationwide hospitalization records found that women have a greater likelihood of developing TTC (Odd ratio of 8.8).⁶ The overall frequency of TTC was calculated to be 5.2 per 100,000 in women and 0.6 per 100,000 in men. Regarding absolute number of admissions, 6,178 (90.4%) were women and 660 (9.6%) were men. Also, they noted that women >55 years old had 4.8 times greater odds of developing TTC when matched

with women <55 years old.

A hallmark of TTC is complete reversibility of the LV contraction abnormalities, new LBBB or QTc prolongation on EKG with slight troponin elevations. The "gold standard" in ruling out a primary coronary obstructive etiology is the use of invasive coronary angiography to exclude coronary artery disorder.⁷

Reported hospital mortality ranges from 0 to 8%, and men had more than two-fold greater mortality than women.^{4,8} Patients with "secondary" TTC have a two- to tenfold higher mortality than those with "primary" TTC. Among hospital deaths, the cause in 62% of cases was related to underlying medical comorbidities, while in 38%, it was directly related to the cardiac complications, mainly caused by refractory cardiogenic shock or ventricular fibrillation.⁹

TTC has widely been considered a somewhat benign condition as many cases recover without complications. However, TTC patients are susceptible to serious complications such as congestive heart failure (12-45%), pulmonary edema (8 to 20%), and cardiogenic shock (4-20%) which is associated with increased short and long-term mortality rates.¹⁰

The previous 3 cases of TTC in renal transplant patients presented with a range of symptoms from anxiety, tachycardia, to cardiac arrest. Many had elevated troponin, left bundle branch block, and all echocardiograms had evidence of Takotsubo. They were all treated with medical management compared to our patient who required Impella placement. Like all previous cases, our patient recovered completely.

Conclusion

Perioperative cases of patients with TTC present with evidence of heart failure, arrhythmias, or cardiac arrest. Thus, one must consider TTC when any of these signs and symptoms occur. Given the nonspecific symptoms and signs after renal transplantation, a high index of suspicion is necessary for detection. A key feature of TTC is recovery of normal cardiac function.

FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Dr. Terra Pearson at tepearson@mcw.edu.

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Development of a Novel Clinical Decision Support System for Older Adult Patients with Traumatic Brain Injury



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Traumatic brain injury is a leading cause of death and disability in geriatric patients.¹ Falls are the most common mechanism of injury in the elderly, with the most frequent injuries being hip fractures and traumatic brain injury (TBI).² Accounting for 32.7% of older adult trauma, TBI is the most common traumatic injury in older trauma patients and the leading cause of injury-related death and disability. Older adult patients have more hospital admissions for TBI and higher TBI-related disability and mortality.³ TBI presents different challenges in the geriatric population because this population has a greater likelihood of having multiple pre-existing medical conditions when compared to younger patients.⁴ 60% of TBI patients over 65 years old have a good recovery, while 40% suffer from prolonged loss of independence and disability. Geriatric TBI patients have higher rates of complications and death, as well as slower recovery.⁵ Efforts to reduce this burden have been hindered by the lack of health-related quality of life predictive models and validated TBI assessment instruments. Existing prediction models for quality-of-life outcomes have poor performance and are difficult to use clinically. Improving care for older adults with serious illness is a public health priority because 1) it affects large numbers of people in Wisconsin, 2) it can reduce unwanted invasive treatments and improve quality of life. This project aims to predict long-term quality of life after injury using patient factors available very early after injury. These predictions will then be shared with patients and caregivers to inform treatment decisions.

The Advancing a Healthier Wisconsin KL2 grant will utilize multidisciplinary skills to optimize the quality of life for older adult trauma patients. This work will help support healthy minds in Wisconsin by improving the quality of life of older adults after traumatic brain injury. This difficult and complex problem requires changing hospital practices and will only be accomplished through a collaboration of clinicians, researchers, patients, their family and our community. Given high treatment burdens and frequency of poor prognosis, seriously injured older adults would benefit from communication interventions that clarify patients' goals, alleviate conflict in

the ICU, and reduce unwanted invasive procedures for dying patients. This work will improve the way providers, patients and families communicate with each other during hospitalization after traumatic injury. We previously used logistic regression to develop three preliminary predictive models, collectively known as Traumatic Brain Injury Patient Reported Outcome (TBI-PRO). These models use approximately 1,300 patients in the Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) databank for a binary Pt-QOLIBRI score (Figure 1). The area under the receiver operating characteristic (AUROC) is a performance metric that is used to evaluate classification models.

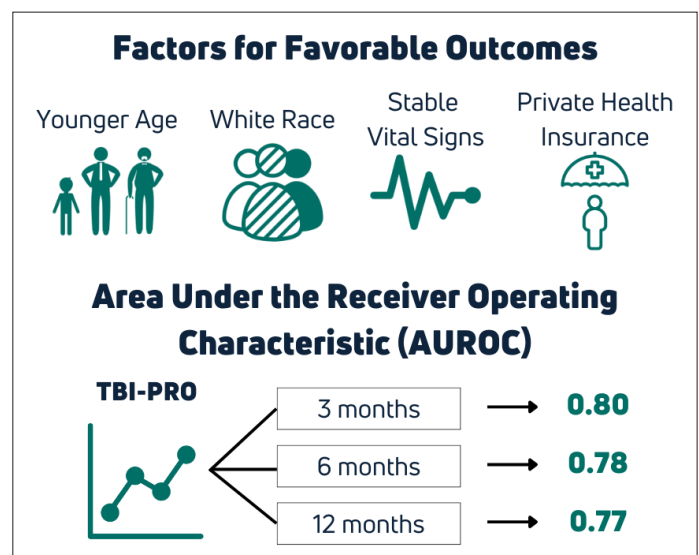


Figure 1: TBI-PRO Mobile Model.

The foundation for this proposal is based on preliminary studies using the patient Quality of Life After Brain Injury (Pt-QOLIBRI) outcome measures. The project will utilize readily available early in-hospital variables to predict long-term quality of life after injury using a down-

Traumatic Brain Injury (TBI)

Enter Age:

Enter Vital Signs:

Used Incident to Arrival Time

SBP (Lowest on day 0)

Number of reactive pupils (lowest on day 0)

Enter Laboratory and Imaging Results:

PTT (Highest on day 0)

Potassium (Lowest on day 0)

Sodium (Highest on day 0)

Creatinine (Highest on day 0)

Urea (Highest on day 0)

Hematocrit (Lowest on day 0)

Figure 2: TBI-PRO Mobile Application

ate a comprehensive decision-support tool to predict a patient-centered quality of life outcome. Although the highest rates of TBI visits, hospitalizations, and deaths occur in older adults, many respond well to aggressive trauma treatment and post-hospitalization rehabilitation. Therefore, it is critical to identify patients with a high likelihood of favorable or unfavorable outcomes, and ultimately reduce the inappropriate withdrawal of aggressive care and use of non-beneficial treatments.⁶ Without development of improved prognostic models, providers will continue to perform non-beneficial interventions and early withdrawal of life-sustaining therapies resulting in loss of quality-adjusted life years, provider burn-out and unnecessary cost.⁷ Currently, in-hospital decisions made with patients, families, and physicians lack informed knowledge of treatments and accurate assessment of long-term prognosis. According to surveys, older people generally want to stay in their own home for as long as possible with the goal of preserving their qual-

ity of life.⁸ Quality of life has many contributing factors including absence of distressing physical symptoms, emotional well-being, quality of close interpersonal relationships, and satisfaction with medical and financial aspects of treatments.⁹ This research will help achieve goal-concordant care, thus optimizing quality of life while avoiding non-beneficial procedures, prolonged hospitalization, additional hospital costs and inappropriate early transition to comfort cares.

loadable free mobile application (Figure 2). Due to cognitive impairment, many severely injured TBI patients are unable to participate in surveys, necessitating the use of a caregiver to report their quality of life through a proxy measure (Proxy-QOLIBRI). How exactly the models can be optimized and applied using patient and proxy measures are questions that this proposal begins to address. The overarching goal of this research is to create

ity of life.⁸ Quality of life has many contributing factors including absence of distressing physical symptoms, emotional well-being, quality of close interpersonal relationships, and satisfaction with medical and financial aspects of treatments.⁹ This research will help achieve goal-concordant care, thus optimizing quality of life while avoiding non-beneficial procedures, prolonged hospitalization, additional hospital costs and inappropriate early transition to comfort cares.

FOR ADDITIONAL INFORMATION on this topic, visit mcw.edu/surgery or contact Dr. Rachel Morris at ramorris@mcw.edu.

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Thoughts at the Scrub Sink: Major League Surgery



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I recently attended the 79th Annual Meeting of the Central Surgical Association where the keynote speaker was Milwaukee Brewers manager Craig Counsell. He spent about an hour reflecting on life, baseball (including recounting the story behind how the “chicken runs at midnight” – well worth a Google search for those who may not be familiar with it) and participating in a question-and-answer session with the attendees. What stood out was his candid discussion of the challenges he faced throughout his career and how they continue to shape his approach today. And how many of those challenges parallel what we encounter daily as a team in the operating room. It left me wondering: is there an opportunity to improve surgical care in the operating room by adopting some of the experiences he has used to become the winningest manager in Milwaukee Brewers’ history?



Douglas B. Evans MD, Roger Caplinger, and Craig Counsell at the CSA 79th Annual Meeting.

#1: Authenticity and trust

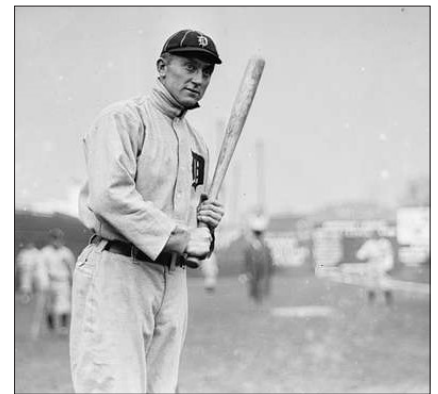
As of July 1, 2022, there have been 20,141 individuals that have played professional baseball in the MLB.¹ During a typical season, each team has about 500 employees.² Regardless of how you split the math, the number of people that have an opportunity to support a professional athletic team (including administration, staff, players) is small. The best of the best. For each player or staff member to perform at their best requires trust in everyone’s own unique process to achieve it. It also means providing room for team members to showcase their real personality and creating space for authenticity in individual interactions. Above all, the highest performing baseball teams blend the immense talent of the individual pieces for the better of the whole. Enhancing a culture of trust in the operating room through authenticity, logic, and empathy is an extension of the type of teaming already happening daily in our ORs and can improve care.

#2: A serious commitment to wholistic player health

To play 162 games in 187 days is an extremely rigorous schedule, both physically and mentally. This has ushered in a new emphasis on player recovery that includes a commitment to injury prevention through biomechanical analytics and individualized training programs.³ Major investments in new technology, tools, and science all have re-shaped the approach to keeping teams in optimal condition, both during and after the season. Applying this approach in surgery can provide a template to develop programs that help protect the workforce and improve the wholistic health of the operating room staff.

#3: Dealing with “slumps”

Ty Cobb holds the career record for batting average at 0.366 over 24 seasons. A 36.6% success rate at almost anything related to the operating room would undoubtedly be considered less than ideal. Still, we can learn a lot from how MLB players manage slumps during a season. While Craig Counsell did acknowledge working through slumps was an “unsolved mystery,” he did have some insight into combating them. Most importantly, it requires letting go of small mistakes and protecting against allowing them to become bigger ones.



Ty Cobb, 1910.⁵

It is an easy argument to make to adopt some of these principles into our day-to-day in the operating room. After all, there are few environments (if any) on the planet where the stakes are higher. There are about 6,000 hospitals in the United States. Of these, about 50 are academic, level 1 trauma, and transplant centers with 600+ beds, perform >10,000 surgical procedures annually, and have over 30 operating rooms.⁴ F&MCW Froedtert Hospital is one of these hospitals – we are the “major league” when it comes to surgical care.

References

1. Baseball Almanac, Inc. <https://www.baseball-almanac.com/players/ballplayer.shtml>.
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3. Papadakis, Z., Padgett, R. N., Stamatis, A. & Karasch, R. A. Baseball performance via the lens of anthropometric testing, fitness metrics, and statistics: a longitudinal cross-sectional study. *Curr. Orthop. Pract.* 32, 151 (2021).
4. AHA Annual Survey Database TM. AHA Data <https://www.ahadata.com/aha-annual-survey-database>.
5. Library of Congress, Prints & Photographs Division, [LC-DIG-ggbain-08006]

Department of Surgery 2022-2023 Fellows

We are thrilled to have the following fellows as a part of MCW Surgery for the upcoming year!

Acute Care Surgery Fellowship

Kathryn Haberman, MD

Advanced GI, MIS & Bariatric Surgery Fellowship

Thomas Xu, MD

Cardiothoracic Surgery Fellowship

Joshua Melamed, MD
Austin Rogers, MD

Clinical Psychology Fellowship

Sydney Timmer-Murillo, PhD

Complex General Surgical Oncology Fellowship

Chad Barnes, MD
Ricardo Bello, MD, MPH

Endocrine Surgery Fellowship

Patrick Hangge, MD

Pediatric Surgery Fellowship

Caroline Maloney, MD, PhD

Alexander Peters, MD, MPH

Surgical Critical Care Fellowship

Nathan Carlson, MD
Isaac Hanson, DO
Brittney Lemon, DO

Surgical Critical Care Fellowship - Pediatric Track

Zachary Morrison, MD

Vascular Surgery Fellowship

Mohammad Rajaei, MD
William Sheaffer Sorrells, MD

Blessing of Staff and Patient in Advance of Surgery

The following nondenominational prayer is provided by the Froedtert & Medical College of Wisconsin Spiritual Services Department, which offers spiritual and emotional support to patients, visitors, and staff. The Spiritual Services Department respects multi-cultural and multi-faith differences and provides spiritual care according to a patient's preference.

May it be Your will to bless the cares of this wonderful staff as they work so diligently and with much kindness to bring healing to the precious lives entrusted to their care.

Help them to use their talents and abilities to care today for this patient and every day for all of their patients – to the very best of their ability, with great love, wisdom, and compassion.

May each member of the team be lifted up and feel blessed with a sense of genuine meaning and purpose through knowing that they are using their gifts to bring healing and life to so many.

In the merit of the staff members' good works, we ask You to bless them, their families and their loved ones. Keep them safe from all harm, and bring to them genuine peace and prosperity.

This morning, we beseech You to bestow a complete and speedy recovery upon this patient. May today's surgery be safe and successful. May it be Your will that all of the disease be removed from this patient's body and that they recover well and speedily from the operation. May they be blessed with good health and length of days.

Please bless this person and all of the patients in this hospital with healing, strength, and a complete and speedy recovery – and the ability to continue to use their talents and abilities to benefit the world and to serve you.

And, may you bless our world with Peace. Amen.

To refer a patient or request a transfer/consultation, please use the references below:

Adult Patients

All Non-cancer Requests
Referrals: 800-272-3666
Transfers/Consultations:
877-804-4700
mcw.edu/surgery

Clinical Cancer Center
Referrals: 866-680-0505
Transfers/Consultations:
877-804-4700

Pediatric Patients

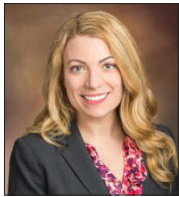
Referrals/Transfers/
Consultations: 800-266-0366
Acute Care Surgery:
414-266-7858

New Faculty

Leading the Way

Division of Congenital Heart Surgery

Tracy R. Geoffrion, MD, MPH



Tracy Geoffrion, MD, MPH, will join the Department of Surgery faculty in October as an Assistant Professor of Surgery. She recently completed her Congenital Cardiothoracic Surgery fellowship at Children's Hospital of

Philadelphia where she also completed a post-doctoral research fellowship. Originally from Texas, she received her medical degree from University of Texas Health Science Center San Antonio. She then completed General Surgery residency and Cardiothoracic Surgery fellowship at University of Texas Southwestern Medical Cen-

ter. Dr. Geoffrion also holds a Master's of Public Health from Dartmouth, with a focus on Healthcare Delivery Science. She is active in research and serves on the Editorial Boards for *Annals of Thoracic Surgery* and the *Journal of Thoracic and Cardiovascular Surgery*. When not working she enjoys exercising, traveling, downhill skiing, trying new restaurants, reading historical fiction, and spending time with friends and family. She will provide clinical care to patients on the Congenital Heart surgery service at the practice locations serviced by the division of Congenital Heart Surgery.

Division of Minimally Invasive & Gastrointestinal Surgery

Wen Hui Tan, MD



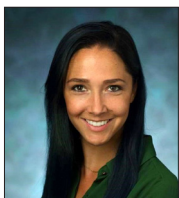
Wen Hui Tan, MD, will join the Department of Surgery faculty in October as Assistant Professor of Surgery. Dr. Tan recently completed a Minimally Invasive/Bariatric Surgery Fellowship in the MCW Department of Surgery,

Division of Minimally Invasive and Gastrointestinal Sur-

gery. Dr. Tan received her medical degree from Washington University in St. Louis School of Medicine where she also completed her general surgery residency at Barnes Jewish Hospital. She will provide clinical care to patients on the Minimally Invasive and GI Surgery service at Froedtert Hospital and the Zablocki VA Medical Center.

Division of Surgical Oncology

Alexandra C. Istl, MD, MPH



Alexandra C. Istl, MD, MPH, FRCS, Assistant Professor of Surgery, joined the Department of Surgery faculty in September from Johns Hopkins Hospital and the Johns Hopkins University School of Medicine, where she re-

cently completed a Complex General Surgical Oncology fellowship. She received her medical degree from the Schulich School of Medicine and Dentistry at Western

University in London, Ontario and remained there for general surgery residency training at the London Health Sciences Centre. Dr. Istl completed her Master's degree in Public Health (Epidemiology and Biostatistics) at the Johns Hopkins University Bloomberg School of Public Health. Dr. Istl will provide clinical care of patients on the Surgical Oncology service at Drexel Town Square Cancer Center and Froedtert Hospital.

Nikki K. Lytle, PhD



Nikki K. Lytle, PhD, will join the Department of Surgery faculty in October as Assistant Professor of Surgery and will conduct her research as a member of the MCW LaBahn Pancreatic Cancer Program. She will hold a secondary appointment in the Department of Pharmacology and Toxicology and will also be a faculty member of the MCW Cancer Center. Dr. Lytle graduated from

Willamette University in Oregon and completed a PhD

at University of California, San Diego in the lab of Dr. Tannishtha Reya. During that time, she made seminal contributions in the understanding of the role of the RNA binding protein and stem cell marker, Musashi, in pancreatic cancer progression. She is currently a postdoctoral fellow at the Salk Institute for Biological Studies in La Jolla, California in Geoffrey Wahl's lab, where she has been studying mechanisms of therapeutic resistance.

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