

UW Medicine

DEPARTMENT OF SURGERY

Presents



2015 RESEARCH DAY AND
21ST ANNUAL
HELEN & JOHN SCHILLING
LECTURE

UW TOWER AUDITORIUM
4333 BROOKLYN AVE NE
SEATTLE, WA 98105

FRIDAY, FEBRUARY 27, 2015

UW Medicine

AGENDA

- 7:00am Breakfast & Registration
- 7:30am Welcome: **Carlos A. Pellegrini, MD, FACS, FRCSI (Hon.)**, The Henry N. Harkins Professor and Chair, Department of Surgery
- 7:35am Introduction: **David R. Flum, MD, MPH**, Professor and Associate Chair for Research, Department of Surgery
- 7:45am **Ravi F. Sood, MD**: Genome-wide association study of post-burn hypertrophic scarring identifies a novel protective variant
- 8:00am **Angelo B. Lipira, MD**: Patient Factors Associated with Complications within 30 Days of Hand Surgery; An Analysis of 9,969 Patients Using the 2006-2011 ACS-NSQIP Datasets
- 8:15am **Meghan R. Flanagan, MD**: Adjuvant Endocrine Therapy in Patients with Ductal Carcinoma in situ in the National Cancer Database
- 8:30am **Damien W. Carter, MD**: MC1R Gene Polymorphisms are Associated with Burn Wound Infection and Acute Systemic Inflammatory Response after Burn Injury
- 8:45am **Katherine Flynn-O'Brien, MD**: Mortality after Emergency Department Thoracotomy For Pediatric Blunt Trauma: Analysis of the National Trauma Data Bank 2007-2012
- 9:00am **Poster Session 1**
- 9:35am **H. Jonathan Chong, MD**: Timing of Microsurgical Breast Reconstruction is Not a Risk Factor For The Development Of Complications
- 9:50am **Chris R. Burke, MD**: Hybrid Repair of the Aortic Arch
- 10:05am **Trina Das, PhD**: Rio Kinase 3 Over Expression Promotes Hepatocellular Carcinoma Invasion Through Induction of Epithelial Mesenchymal Transition and a Potential Link to Wnt/B-Catenin Pathway Activation
- 10:20am **Lacey N. LaGrone, MD, MA**: A Systematic Review of Global Implementation of the World Health Organization Essential Trauma Care Publications
- 10:35am Recognition: **Alexander W. Clowes, MD**
- 10:50am **Poster Session 2**
- 11:25am Faculty Presentation: **Adam B. Goldin, MD, MPH**
- 11:40am **Vlad V. Simianu, MD**: Surgeon Behavior After Anastomotic Leak in Colon Surgery
- 11:55am **Shakirat Oyetunji, MD**: Lysyl-Like Oxidase 2 (Loxl2) is an Oncogenic Driver Of Malignancy Regulated by Mir-145 in Tobacco-Associated Esophageal Adenocarcinoma
- 12:10pm **Deepika Nehra, MD**: Acute Rehabilitation after Trauma: Does it Make a Difference?
- 12:25pm **Lunch**
- 1:05pm **Poster Session 3**
- 1:35pm Faculty Presentation: **Giana H. Davidson, MD, MPH**
- 1:50pm **Brodie Parent, MD**: A Novel Diagnostic and Prognostic Tool in Critically-Ill Trauma Patients: Metabolomic Profiling Reveals Pervasive Changes
- 2:05pm **Kevin M. Riggle, MD**: Enhanced Cyclic-AMP Induced Protein Kinase A Activity in Fibrolamellar Hepatocellular Carcinoma
- 2:20pm **Morgan K. Richards, MD**: Endoscopic, Laparoscopic, Image-Guided Pediatric Gastrostomy Tube Placement: Improved Outcomes with a Standardized Approach

- 2:35pm **Anne E. Pugel, MD:** Alvimopan Use, Outcomes, and Costs: A Report from the SCOAP CERTAIN Collaborative
- 2:50pm **Closing Remarks:** David R. Flum, MD, MPH, Professor and Associate Chair for Research, Department of Surgery
- 3:00pm **Break**
- 3:30pm **21st Annual Schilling Lecture – Walter J. Pories, MD: “Surgical Research! Really?”**
- 4:30pm Reception
- 5:30pm Adjourn

Poster Session Schedule

Session 1:

- 9:00am **Ali Darehzereshki, MD:** Differential Regenerative Capacity of Neonatal Mouse Hearts After Cryoinjuries
- 9:05am **Lyndsay A. Deeter, MD:** Hospital-Acquired Complications Alter Quality Of Life in Burn Survivors
- 9:10am **Galit Eliahoo, PhD:** Knockout of P27kip1 Enhances Ischemia Induced Collateralization Through a Novel Collateral Pathway
- 9:15am **Harry V. Flaster, MD:** Liver Transplantation Outcomes Among Patients with Inborn Errors of Metabolism: Worth the Risk?
- 9:20am **Suzette G. Miranda, MD:** Outcomes of Ketorolac Administration in Microsurgical Breast Reconstruction

Session 2:

- 10:50am **Shane D. Morrison, MD, MS:** Long-Term Outcomes of Rectosigmoid Neocolporrhaply in Male-To-Female Gender Reassignment Surgery
- 10:55am **Joshua M. Mourot, MD:** Improvement in Pulmonary Function Following Laparoscopic Gastric Bypass for Patients with Interstitial Lung Disease
- 11:00am **Terra Pearson, MD:** Rabbit Antithymocyte Globulin is Associated with Improved Patient and Graft Survival in Liver Transplantation. Experience With 595 Patients at the University of Washington
- 11:05am **Roberto A. Salas Fragomeni, MD:** Clinical Profiling Of BCL-2 Family Members in the Setting of BRAF Inhibition Offers a Rationale for Targeting De Novo Resistance Using BH3 Mimetics
- 11:10am **Max E. Seaton, MD:** Burn Wound Infections Do Not Increase the Risk Of Hypertrophic Scarring

Session 3:

- 1:05pm **Jonathan G. Sham, MD:** Evaluating the Mechanisms of Improved Glucose Homeostasis After Bariatric Surgery in Ossabaw Miniature Swine
- 1:10pm **Janelle D. Sousa, MD:** Completion of Cleft Care: A Single Surgeon’s Experience with Unilateral Cleft Lip and Palate
- 1:15pm **Callie M. Thompson, MD:** Risk Factors for Burn Wound Infection: Data from the Inflammation and The Host Response to Injury Study
- 1:20pm **Robert B. Yates, MD:** Laparoscopic Gastropexy for the Management of Obstructed Gastric Volvulus in High Operative Risk Patients

INTRODUCTION



Carlos A. Pellegrini, MD,
FACS, FRCSI (Hon.)
The Henry N. Harkins
Professor & Chair

Welcome to the Department of Surgery Annual Research Symposium and Schilling Lecture! This year is the 21st anniversary of the Schilling Lecture, which was made possible by a generous gift from the late Helen Schilling in honor of her husband, Dr. John Schilling. The Schillings shared a deep commitment to teaching, scholarship, and research and we are proud to be able to honor this commitment through research-related events such as this.

Each year, the Department of Surgery invites a distinguished leader in surgical research to attend the symposium and give the annual Schilling Lecture, and we are very excited to host this year's distinguished guest, Dr. Walter J. Pories, Professor of Surgery, Biochemistry and Kinesiology at East Carolina University. Dr. Pories will help adjudicate the symposium, then give the Schilling Lecture, titled "*Surgical Research! Really?*" in which he will provide an overview of the development of bariatric surgery and the mechanisms underlying the remission of diabetes and the metabolic syndrome. As a published cartoonist, his talk is certain to be as entertaining as it is informative!

The purpose of this symposium is multi-faceted: it is a forum for bringing together faculty, residents, fellows, students, and friends to share and discuss the impactful research taking place in our Department. It is also an important learning opportunity for residents and fellows to refine their scientific presentation skills through oral and poster presentations, audience Q&A, and feedback from our panel of judges. Finally, we view this day as a celebration—a celebration of the passion for research in our Department. Each and every member of the Department has a role in the success of our research mission, either as mentors or collaborators, and we are extremely thankful for the hard work of our staff, faculty, and trainees who make events like this possible.

Finally, we are happy to announce that we will continue last year's expanded symposium format featuring both podium and poster presentations and assigned discussants for the plenary session. Discussants will open each Q&A session by providing a framework for the presentation and asking each speaker a probing question designed to help teach Q&A preparedness. This evening we will honor all participants and their mentors, and present cash prizes to the top poster and oral presenters.

We are very pleased that you are joining us today as we recognize the hard work of our residents, fellows, and their faculty mentors, and continue the Schilling tradition of celebrating research. We hope you find today's event both informative and engaging!

Sincerely,

Carlos A. Pellegrini, MD, FACS, FRCSI (Hon.)
The Henry N. Harkins Professor & Chair
Department of Surgery
University of Washington

David R. Flum, MD, MPH
Associate Chair for Research, Surgery
Professor, Surgery, Health Services, and Pharmacy
Department of Surgery
University of Washington



David R. Flum, MD, MPH
Associate Chair
for Research
Professor of Surgery

WALTER J. PORIES, MD, FACS



Walter J. Pories, MD, FACS
Professor of Surgery,
Biochemistry and Kinesiology
Brody School of Medicine
East Carolina University
North Carolina

Walter J. Pories, MD, FACS, Professor of Surgery, Biochemistry and Kinesiology at East Carolina University, is a graduate of Wesleyan University in Middletown, Connecticut. He received his MD with Honor at the University of Rochester, where he also completed his surgical training in general and cardiothoracic surgery. He served on the faculties of the University of Rochester, Case Western Reserve until 1977 when he became the founding Chairman of Surgery at East Carolina University (ECU), a position he held for 19 years. He is currently the Director of the Metabolic Surgery Research Group at ECU.

Dr. Pories' major clinical interests have been in nutrition, pediatric and bariatric surgery. His significant research achievements include the discovery that zinc is an essential element and required for wound healing, the development of animal feeds, and the addition of trace elements to parenteral and alimentary formulations. He was the first to describe the use of suction to promote wound healing and the first to perform a cysterna-chili/vena cava anastomosis for congenital absence of the thoracic duct. He was also the first to delineate the full and durable remission of type 2 diabetes following the gastric bypass. Dr. Pories is currently a Principal Investigator for the NIH/NIDDK study, the Longitudinal Assessment of Bariatric Surgery (LABS), as well as others supported by both the NIH and industry.

Dr. Pories has served as the President of the Society for Geochemistry and Environmental Health, the American Society for Metabolic and Bariatric Surgery, the Association of Program Directors of Surgery, the North Carolina Medical Board, the Surgical Review Corporation, the North Carolina Chapter of the American College of Surgeons and as the editor-in-chief or associate editor on a number of journals including Current Surgery, North Carolina Medical Journal, and The Surgical Resident. He is the recipient of a number of research honors, including the Goldwater Award in Nutrition, the McGovern Award, the ECU Lifetime Research Achievement Award and the O. Max Gardner Award, among others. Dr. Pories is also a talented cartoonist and has published over 200 cartoons and illustrations in a wide variety of publications.

He retired from the United States Army with the rank of Colonel after 24 years of service with a Legion of Merit and a Presidential Citation for the performance of the regiment under his command in the first Gulf War.

Dr. Pories lives on a working farm with this wife, Dr. Mary Ann Rose, in eastern North Carolina. They have six children and a variety of livestock and wildlife including a llama and family of bears who roam on the farm's banks of the Tar River.



"I don't need a seat. I'm just here to sign the attendance record..."

ABOUT HELEN & JOHN SCHILLING



Helen & John Schilling

The Helen and John Schilling Endowed Lectureship was established by the late Helen Schilling to bring distinguished scholars to the Department of Surgery at the University of Washington, and to enhance the Department's commitment to the highest standards of patient care, teaching, research and scholarship. It was Mrs. Schilling's wish that the lectureship be in honor of her husband, John.

Dr. Schilling devoted his life to academic medicine in a career spanning 50 years. He was born and raised just outside Kansas City, Missouri, and at the age of 15 entered Dartmouth College. After graduating from Dartmouth in 1937, he attended Harvard Medical School as a member of the class of 1941, the last class to graduate before World War II. In the six months before the start of his internship and residency at the Roosevelt Hospital in New York City, he signed on as a ship's doctor on the schooner Effie M. Morrissey for a scientific expedition to the Arctic sponsored by the U.S. Bureau of Standards. After a number of perilous adventures along the Greenland coast and in the Hudson Straits, he returned to New York and started his training in general surgery. He joined the surgical

staff at the University of Rochester in 1945 where he began his life long work on wound healing. His career at Rochester was interrupted for several months by a stint in the central Pacific (Eniwetok) to participate in the study of flash burns as part of the atom bomb tests and the Manhattan Project. Subsequently he joined the Air Force as a volunteer and set up a surgical department at the new School of Aviation Medicine in San Antonio.

In 1956 Dr. Schilling was invited to be the chief of the first full-time department of surgery in the new medical school at the University of Oklahoma. He was successful in recruiting a number of outstanding junior faculty, many of whom have gone on to become chairmen. In addition to his administrative responsibilities, he maintained an extensive research program in wound healing in collaboration with Dr. Betty White. At the end of 18 years Dr. Schilling and his faculty had trained 75 surgeons from Oklahoma and adjoining states and had established a department known for its academic accomplishments.

Dr. Schilling came to the University of Washington in 1974 as a senior investigator and, upon the sudden resignation of the chairman, was asked to take over the management of the Department of Surgery. Thus began his third chairmanship which lasted eight years until his retirement. His first responsibility was to recruit faculty to fill the many vacancies, a task he achieved after several stormy years. Upon his retirement in 1983, he had recruited 41 new faculty members and graduated a total of 40 chief residents.

His career in academic surgery was marked by a devotion to patient care and teaching, as well as research. But, despite his commitment to the profession, Dr. Schilling still found time to engage in other activities. From his early childhood, he enjoyed the outdoors and had become an expert tennis player, skier, and fly fisherman; he always believed that one's life work should be punctuated by intervals of travel and recreation.

Helen Schilling shared with her husband both the non-academic as well as the academic side of his life. They first worked together in Rochester and continued their association through the years in Oklahoma and Washington. They were married in 1979. She had a career in newspaper work and administration after graduating from Oberlin College. This dual background enabled her to be his close associate and administrative assistant for 40 years.

JUDGES

Special Guest Judge



Walter Pories, MD
Professor, Brody School of Medicine

Department of Surgery Research Leadership



Carlos A. Pellegrini, MD, FACS, FRCSI (Hon.)
The Henry N. Harkins Professor & Chair



David R. Flum, MD, MPH
Associate Chair for Research, Professor of Surgery

Research Leadership Committee



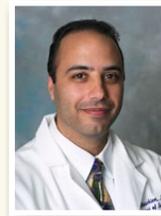
Saman Arbabi, MD, MPH
Professor



Eileen Bulger, MD
Professor



Alexander Clowes, MD
Professor



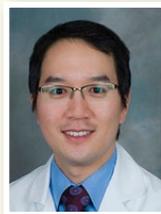
Joseph Cuschieri, MD
Professor



Nicole Gibran, MD
Professor



Anne Hocking, PhD
Research Assoc. Professor



Jason Ko, MD
Assistant Professor



Ronald Maier, MD
Professor, Division Chief



Michael Mulligan, MD
Professor



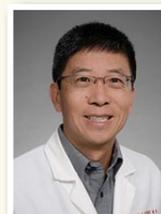
Grant O'Keefe, MD, MPH
Professor



Kimberly Riehle, MD
Assistant Professor

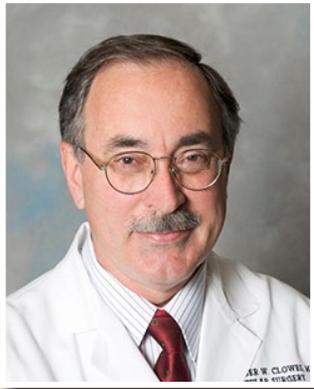


Robert Sawin, MD
Professor, Division Chief



Raymond Yeung, MD
Professor

FEATURED DEPARTMENT OF SURGERY FACULTY



Alexander W. Clowes, MD
Professor, Division of Vascular Surgery

Dr. Clowes is a Professor in the Division of Vascular Surgery and holder of the V. Paul Gavora - Helen S. and John A. Schilling Endowed Chair in Vascular Surgery, and the founder of the annual Schilling Lecture. His research focuses on the mechanisms of stenosis and restenosis after vascular reconstruction, and his primary goal is to understand the factors, including genetic differences, that stimulate and inhibit the growth of cells in the vessel wall, and to develop new strategies for the pharmacological control of intimal hyperplasia and luminal narrowing after vascular injury. Dr. Clowes has been continuously funded by National Institutes of Health (NIH) for over 30 years and has published over 200 peer-reviewed articles. He has received numerous awards for his contributions to science, including the Sheen Award for outstanding achievement in medical science, and the Flance-Karl Award for fundamental contributions in the biology of vascular disease.

Adam B. Goldin, MD, MPH
Associate Professor, Division of Pediatric General Surgery

Dr. Goldin's research interests include clinical outcomes and quality of care in pediatric surgery. He seeks to question the assumptions upon which current practice decisions are based, and identify appropriate historical and contemporary processes and outcomes in order to improve care. Dr. Goldin is a member of the American Pediatric Surgical Association Outcomes and Evidence-Based Medicine Committee, and the chair of the subcommittee on surveys. He also serves as the chair of the pediatric surgery pilot project of the Washington State Surgical Care and Outcomes Assessment Program. During his surgical training here in the UW Department of Surgery, Dr. Goldin undertook a clinical research fellowship under the direction of Robert Sawin, MD, Chief and Professor in the Division of Pediatric Surgery, and Dr. David Flum, Professor in the Division of General Surgery, while pursuing his Master in Public Health. Recently, he has been working on the Children's Surgical Task Force, identifying resources necessary for safe surgery in infants and children.



Giana H. Davidson, MD, MPH
Assistant Professor, Division of General Surgery

Dr. Davidson's research focuses on improving the health of patients receiving specialized post-acute care in skilled nursing facilities (SNFs) following hospitalization. She has led a multi-disciplinary collaborative effort with leaders from surgery, medicine, geriatrics, palliative care, and critical care targeted for research and quality improvement initiatives. This collaborative, Improving Nursing Facility Outcomes using Real-Time Metrics (INFORM), evaluates variability in patient, structural, and process factors that contribute to patient-centered outcomes with the goal of better understanding the post-hospital period and creating benchmark standards of care for acute care patients. She is an associate member of The Harborview Injury Prevention Research Center (HIPRC) and also works with the Surgical Outcomes Research Center (SORCE). During her surgical residency in UW Department of Surgery she completed a two-year research fellowship in the Pediatric Injury Research T32 program under Principal Investigator Frederick Rivara, MD, MPH.

PLENARY SESSION ABSTRACTS

IN
PRESENTATION
ORDER

RAVI F. SOOD, MD
ANGELO B. LIPIRA, MD
MEGHAN R. FLANAGAN, MD
DAMIEN W. CARTER, MD
KATHERINE FLYNN-O'BRIEN, MD
H. JONATHAN CHONG, MD
CHRIS R. BURKE, MD
TRINA DAS, PhD
LACEY N. LAGRONE, MD, MA
VLAD V. SIMIANU, MD
SHAKIRAT OYETUNJI, MD
DEEPIKA NEHRA, MD
BRODIE PARENT, MD
KEVIN M. RIGGLE, MD
MORGAN K. RICHARDS, MD
ANNE E. PUGEL, MD



Ravi F. Sood, MD

Research Resident

Hometown: Chicago, IL

Medical School: University of Chicago

Research Interests: Hypertrophic scarring, genetic epidemiology

Faculty Mentor

Nicole S. Gibran, MD

GENOME-WIDE ASSOCIATION STUDY OF POST-BURN HYPERTROPHIC SCARRING IDENTIFIES A NOVEL PROTECTIVE VARIANT

Sood RF, Hocking AM, Muffley LA, Ga M, Honari S, Reiner AP, Gibran NS

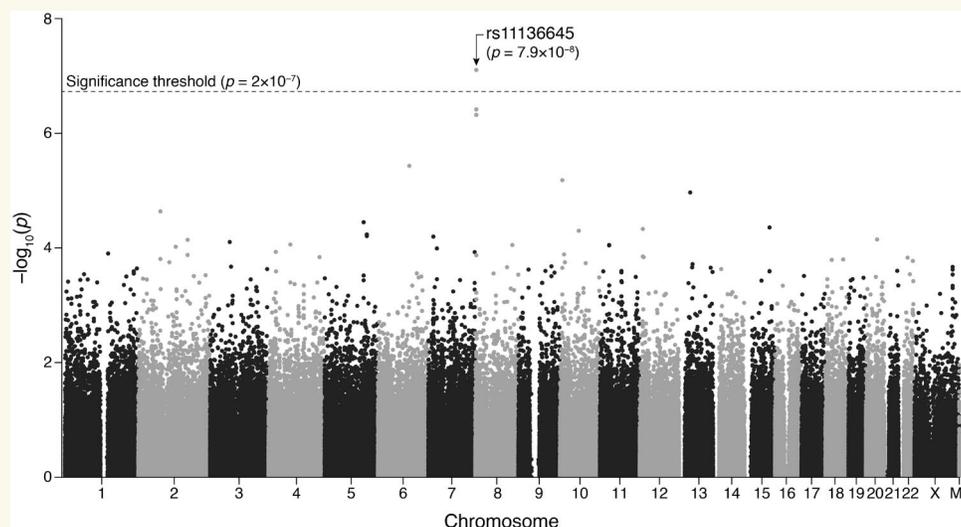
Background: Burn injuries and other partial-thickness wounds often lead to hypertrophic scarring (HTS), a debilitating sequela with racial predisposition that suggests a genetic mechanism. We sought to identify single-nucleotide polymorphisms (SNPs) associated with HTS.

Methods: We conducted a genome-wide association study in a prospective cohort of adults admitted with deep-partial-thickness burns. Scar severity was assessed over time using the Vancouver Scar Scale (VSS), and DNA was genotyped with a >500,000-marker array. We performed association testing of SNPs with minor allele frequency (MAF) >0.01 using linear regression of VSS height score on genotype adjusted for patient- and injury characteristics as well as population substructure. Genome-wide significance was based on Bonferroni correction for multiple testing.

Results: Of 538 patients (median age 40 years, median burn size 6.0% body surface area), 71% were male and 76% were white. The mean VSS height score was 1.2 (range: 0–3). Of 289,639 SNPs tested, a variant in the “CUB and Sushi multiple domains 1” (CSMD1) gene (rs11136645; MAF = 0.49), was significantly associated with decreased scar height (regression coefficient = -0.23, $p = 7.9 \times 10^{-8}$; see Figure).

Conclusions: We report the first SNP associated with reduced severity of post-burn HTS. A common intron variant in the CSMD1 gene is associated with decreased scar height, suggesting an anti-fibrogenic effect. CSMD1 is a known tumor-suppressor implicated in colorectal cancer, underscoring the commonality of morphogenetic responses.

Figure. Manhattan plot of p -values for 289,639 SNPs demonstrating a single variant (rs11136645) significantly associated with post-burn scar height. Dashed line indicates genome-wide significance level. MT = mitochondrial DNA.





Angelo B. Lipira, MD

Plastic Surgery, R5

Hometown: Saint Joseph, MO

Medical School: Washington University

Research Interests: Plastic surgery, hand surgery, outcomes analysis

Faculty Mentor

Jason H. Ko, MD

PATIENT FACTORS ASSOCIATED WITH COMPLICATIONS WITHIN 30 DAYS OF HAND SURGERY; AN ANALYSIS OF 9,969 PATIENTS USING THE 2006-2011 ACS-NSQIP DATASETS

Lipira AB, Tatman PD, Ko JH

Background: The ACS-NSQIP database collects detailed and validated data on patient demographics, co-morbidities, and 30-day postoperative outcomes on patients undergoing operations in most subspecialties. This dataset has been previously used to delineate specific complication risks and risk factors in a number of surgical subspecialties, but has not yet been used for hand surgery. While the risk of early complications following hand surgery is generally believed to be low, it is important to define these risks quantitatively, and to identify patient groups who are at higher risk for complications so that preventive measures can be employed.

Methods: ACS-NSQIP data from 2006-2011 was queried using 293 hand-specific CPT codes. Descriptive statistics were calculated for the population, and potential risk factors and patient characteristics contained within the NSQIP database were analyzed for their association with complications in the 30-day postoperative period using both univariate and multivariate analyses. The most common complications were identified, and significantly associated variables were determined.

Results: 204 hand-specific CPTs were represented in the data. Of these, 81 resulted in at least one complication. The overall 30-day complication rate for hand surgery was 2.54%. In univariate analysis, older age, diabetes, COPD, CHF, atherosclerosis, steroids, bleeding disorder, emergency surgery, increasing ASA class, increasing wound class, and transfusion were associated with significantly higher relative risk of complications. In the multivariate model, male sex, bleeding disorder, emergency surgery, increasing ASA class, increasing wound class, and transfusion were associated with significantly higher relative risk. There was no significant association with race, anesthesia type, or operative time. The most common complications were SSI and bleeding requiring transfusion.

Conclusions: This study utilized a large, prospective national database to characterize the 30-day complication profile and risk factors for surgery of the hand. Overall, the incidence of complications is low, approximately 2.5%. Overall health status seems to be more important than specific comorbidities in predicting complication risk. The most common complications are listed and quantified. This information is valuable in counseling patients preoperatively, and in identifying groups of patients on whom risk reduction efforts should be focused.



Meghan R. Flanagan, MD

Research Resident

Faculty Mentor

Sara H. Javid, MD

Hometown: Los Altos, CA

Medical School: Albert Einstein College of Medicine

Research Interests: Management of ductal carcinoma in situ, quality improvement and safety

ADJUVANT ENDOCRINE THERAPY IN PATIENTS WITH DUCTAL CARCINOMA IN SITU IN THE NATIONAL CANCER DATABASE

Flanagan MR, Rendi MH, Gadi VK, Calhoun KE, Gow KW, Javid SH

Background: Adjuvant endocrine therapy (ET) has been shown to reduce the risk of second breast cancer events among women with ductal carcinoma in situ (DCIS), particularly among women with estrogen receptor positive (ER+) disease treated with breast conserving surgery (BCS). There is no population-level evaluation of ET use in DCIS patients subsequent to standardized reporting of ER status in cancer registries in 2004.

Methods: We conducted a retrospective cohort study of women with unilateral DCIS in the National Cancer Database between 2005 and 2011. Patient, tumor and treatment characteristics, as well as temporal trends associated with recommendation and receipt of ET were evaluated.

Results: Among 132,948 DCIS patients, clinician recommendation of ET increased from 44% in 2005 to 54% in 2011 for all patients, and 54% to 63% for ER+ patients. 11% (11,758) of women who were recommended ET declined therapy. Receipt of ET after BCS in ER+ patients increased from 49% to 54% (p-trend <0.001), and decreased among ER- patients (11% to 7.5%, p-trend=0.001). Age, year of diagnosis, race, co-morbidity index, insurance status, DCIS grade, ER status, surgical procedure, margin status and receipt of adjuvant radiation were associated with receipt of ET on univariate analysis. On multivariable analysis, black race was positively associated with receipt of ET (Table 1). Very young (<40 years) and older (≥60 years) patients were less likely to receive ET than patients aged 50-59 years old. Patients with public insurance were less likely to receive ET than patients with private insurance (OR 0.88, 95% CI 0.85-0.91). Those patients who underwent unilateral mastectomy were also less likely to receive ET when compared to those who underwent BCS (OR 0.87, 95% CI 0.84-0.91).

Conclusions: Among women treated for DCIS between 2005-2011, clinician recommendations for ET increased among all patients, but receipt of therapy increased only 5% among patients undergoing BCS for ER+ DCIS, the group of women most likely to benefit from its use. Further research is needed to determine the causes of variation and decision-making factors in the recommendation and receipt of ET.



Damien W. Carter, MD

Critical Care Fellow

Faculty Mentor

Nicole S. Gibran, MD

Hometown: Oakland, CA

Medical School: University of Illinois

Research Interests: Burn immunology, translational burn research

MC1R GENE POLYMORPHISMS ARE ASSOCIATED WITH BURN WOUND INFECTION AND ACUTE SYSTEMIC INFLAMMATORY RESPONSE AFTER BURN INJURY

Carter DW, Sood RF, Seaton ME, Muffley LA, Hocking AM, Honari S, Gibran NS

Background: The Systemic Inflammatory Response Syndrome (SIRS) is known to be associated with organ failure and infectious complications after severe burn injury. Recent evidence has linked melanocortin signaling to anti-inflammatory and wound-repair functions, with mutations in the melanocortin 1 receptor (MC1R) gene leading to increased inflammatory responses. Our group has previously demonstrated that MC1R gene polymorphisms are associated with post-burn hypertrophic scarring. Thus, we hypothesized that certain MC1R gene polymorphisms would be associated with increased burn-induced SIRS and increased infectious complications.

Methods: We enrolled adults (>18 years of age) who sustained >20% TBSA partial/full thickness burns between 2006-2013. We screened for five MC1R SNPs (V60L, V92M, R151C, R163Q, T314T) by PCR from genomic DNA isolated from blood samples. We performed a detailed review of each patient chart to identify age, sex, race, ethnicity, percent total-body-surface-area burned (%TBSA), burn wound infections (BWI), and 72hr intravenous fluid volume (IVF), the latter a surrogate for a dysfunctional inflammatory response to injury. To examine the association between each MC1R SNP and burn wound infection, we used multivariate Poisson regression with robust standard errors and included age, sex, %TBSA, ethnicity, and race (to control for confounding by population substructure) as adjustment variables. To examine the association between each SNP and 72h IVF, we used linear regression with robust standard errors.

Results: Of 106 subjects enrolled, 82 had complete data for analysis. Of these, 64 (78%) were male, with a median age of 39 and median %TBSA of 30%. A total of 36 (44%) subjects developed burn wound infections. The median total IVF in first 72h was 24.6 L. By multivariate Poisson regression, the R151C polymorphism was a significant independent risk factor for burn wound infection (adjusted prevalence ratio 2.03; 95% CI: 1.21-3.39; $p = 0.007$). By multiple linear regression, the V60L polymorphism was independently associated with increased resuscitation fluid volume ($p = 0.021$).

Conclusions: This is the first study to demonstrate a significant association between genetic polymorphisms and a burn-induced SIRS complication. Our findings suggest that MC1R polymorphisms are important factors leading to dysfunctional responses to burn injury that may predict infectious and inflammatory complications.



Katherine Flynn-O'Brien, MD

Research Resident

Hometown: Albuquerque, NM

Medical School: University of New Mexico

Research Interests: Pediatric trauma and quality care indicators

Faculty Mentor

Frederick P. Rivara, MD, MPH

Department of Pediatrics

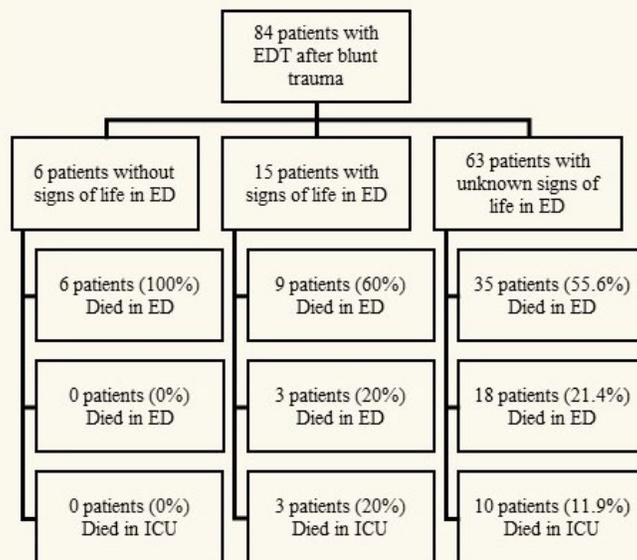
MORTALITY AFTER EMERGENCY DEPARTMENT THORACOTOMY FOR PEDIATRIC BLUNT TRAUMA: ANALYSIS OF THE NATIONAL TRAUMA DATA BANK 2007-2012

Flynn-O'Brien KT, Stewart BT, Fallat ME, Maier RV, Arbabi S, Rivara FP, McIntyre LK

Background: The indications for and likelihood of survival after emergency department thoracotomy (EDT) following blunt trauma in children are not clear. The aim of this study is to examine the survival rate in a national study of pediatric patients with blunt trauma undergoing EDT.

Methods: A retrospective review of the National Trauma Data Bank from 2007-2012 was performed to identify children < 18 years of age who underwent EDT for blunt trauma.

Results: A total of 84 children < 18 years of age were identified as having EDT after blunt trauma. Between 2007 and 2012, EDT was performed at 57 different facilities, with no single facility doing more than two per year. Sixty-five percent of the population was male, with a median age of 15 (IQR 6-17) years. Mean injury severity score (ISS) across all children was 34.2 (SD 20.8), with 56.0% having an ISS of 26-75. Every child died during their hospitalization. Sixty percent of patients died in the emergency department (ED). Of those who survived to the operating room (OR), 65.6% died on the table. Only four children (4.8%) survived more than 24 hours in the intensive care unit (ICU), all of whom expired during their hospitalization. Data for “signs of life” upon arrival was coded starting in 2011, and was available for 21 patients undergoing EDT, of whom 6 (28.6%) had no signs of life.



Conclusions: Based on this limited dataset, there are no survivors after EDT for blunt trauma in the pediatric population over the 6 year period of data captured by the NTDB. Usual indicators for EDT in adults may not apply in children. We conclude the use of EDT for pediatric blunt trauma should be discouraged without compelling evidence of a reversible cause of extremis.



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Plastic Surgery, R5

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Research Interests: Reconstructive microsurgery

Faculty Mentor

Alexander J. Gougoutas, MD

TIMING OF MICROSURGICAL BREAST RECONSTRUCTION IS NOT A RISK FACTOR FOR THE DEVELOPMENT OF COMPLICATIONS

Chong HJ, Sood RF, Chung S, Gougoutas AJ, Mathes DW

Background: Microsurgical breast reconstruction is generally pursued in a delayed manner after completion of mastectomy and adjuvant therapies. In lower-risk patients, immediate reconstruction at the time of mastectomy offers the advantages of combining procedures under one anesthetic, preserving the breast envelope, and improving psychological distress. Another approach is to complete reconstruction in a “delayed-immediate” manner, in which tissue expanders are placed at the time of mastectomy followed by interval reconstruction several weeks later. There are no studies comparing outcomes between these three approaches. We sought to determine whether an association exists between the timing of microsurgical breast reconstruction and the development of complications.

Methods: We conducted a retrospective cohort study enrolling all patients undergoing DIEP (deep inferior epigastric artery perforator) free flap breast reconstruction from March 2010–March 2013. The primary exposure was timing of reconstruction, classified as delayed, immediate, or delayed-immediate. The primary outcome was the development of any breast- or abdominal-site complication. Our secondary outcome of interest was complications resulting in re-operation. Univariate analysis of complication rates was performed using the chi-square test. To control for potential confounders, we also performed Poisson multivariate regression with the following covariates: age, BMI, diabetes, hypertension, smoking, chemotherapy, radiation, operative length, mastectomy type, and laterality of reconstruction (unilateral vs. bilateral).

Results: Of 255 patients enrolled (mean age 49.4 ± 9.1 years), 116 (45.5%) underwent delayed reconstruction, 74 (29.0%) immediate, and 65 (25.5%) delayed-immediate. Across all groups, 176 (69.0%) experienced at least one complication, with 98 flap-related, 111 breast-site, and 71 abdominal-site complications observed. Of these patients, 58 (22.7%) required a return trip to the operating room for the following reasons: breast-site hematoma (28), vascular compromise of the flap (33), and abdominal-site infection (2). By univariate analysis, there was no significant association between timing of reconstruction and the development of any complication (68.1%, 77.0%, and 61.5% for the delayed, immediate, and delayed-immediate cohorts, respectively; $p = 0.14$). Similarly, the rate of complications resulting in re-operation did not vary by timing ($p = 0.06$). After adjusting for potential confounders in a multivariate regression model, we also found no significant association between timing of reconstruction and the development of complications ($p = 0.23$). Compared to delayed reconstruction, the adjusted relative risk for the development of peri-operative complications was 1.12 (95% CI: 0.85-1.49) for immediate reconstruction and 0.89 (95% CI: 0.67-1.18) for delayed-immediate reconstruction. Similarly, after adjusting for potential confounders, we did not detect an association between timing of reconstruction and complications resulting in a return trip to the operating room ($p = 0.40$).

Conclusions: The timing of microsurgical breast reconstruction does not appear to significantly alter the overall risk of peri-operative complications or the risk of more significant complications requiring a return trip to the operating room.



Chris R. Burke, MD

Cardiothoracic Surgery, R4

Faculty Mentor

Matthew P. Sweet, MD

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Research Interests: Aortic Dissection, mechanical circulatory support, extracorporeal membrane oxygenation

HYBRID REPAIR OF THE AORTIC ARCH

Burke CR, Sweet MP, Aldea GS, Pal J, Starnes BW

Background: The surgical treatment of aortic arch pathology remains a formidable challenge. Mortality rates of traditional open repair have been reported as high as 10% in some series. Endovascular treatment of abdominal and descending thoracic aortic pathology is well described, with results equaling, and exceeding in some cases, open repair. This has led some to attempt to translate these endovascular technologies to the aortic arch. These techniques range from “hybrid” repairs to total endovascular stent grafting.

Objectives: We reviewed our series of patients that have been treated for aortic arch pathology with a hybrid repair, namely an open debranching procedure followed by endovascular stenting in the arch with Zone 1 or Zone 0 landing zones. From May 2008 to September 2014, we treated a total of 12 patients in this fashion. All patients were deemed poor candidates for open repair, two were symptomatic and one was ruptured. Seven patients had primary aneurysms of the aortic arch and 5 patients had previously had an ascending aortic replacement for type A dissection and had developed aneurysmal degeneration of their arch.

Results: Technical success was achieved in 11 out of 12 patients. Two patients had concomitant CABG procedures. Ten of 12 patients survived to hospital discharge. Two patients died in the peri-operative period. One patient with a ruptured aneurysm died on the OR table. One patient died on POD 1 due to MI. Six patients were discharged home following their procedure, with 4 patients requiring skilled nursing facility admission. One patient died 3 months post-operatively after a complicated and prolonged recovery. There was one stroke observed in the study period. One patient developed spinal cord ischemia and a transient neurologic deficit, but ultimately fully recovered. There were two myocardial infarctions noted in the study period, one of which was fatal. Two patients developed a type 1A endoleak that are without option for re-intervention. Both aneurysms have remained stable. One patient was lost to follow-up during the study period. Treatment success, defined as aneurysm exclusion and return to pre-op functional status, was achieved in 8 out of 12 patients.

Conclusions: Our results represent a “real world” single center experience using hybrid technologies to treat aortic arch pathology in patients deemed prohibitive risk for open repair. These data indicate that technical success can be achieved using these techniques. Intermediate-term data indicate these patients can survive several years with hybrid repair. However, there is still significant morbidity associated with these challenging patients. Devices and surgical techniques will continue to require refinement in order to optimize results in these difficult clinical scenarios. Further investigation will be needed to assess the results of hybrid repairs with traditional open techniques.



Trina Das, PhD
Transplant Research Fellow

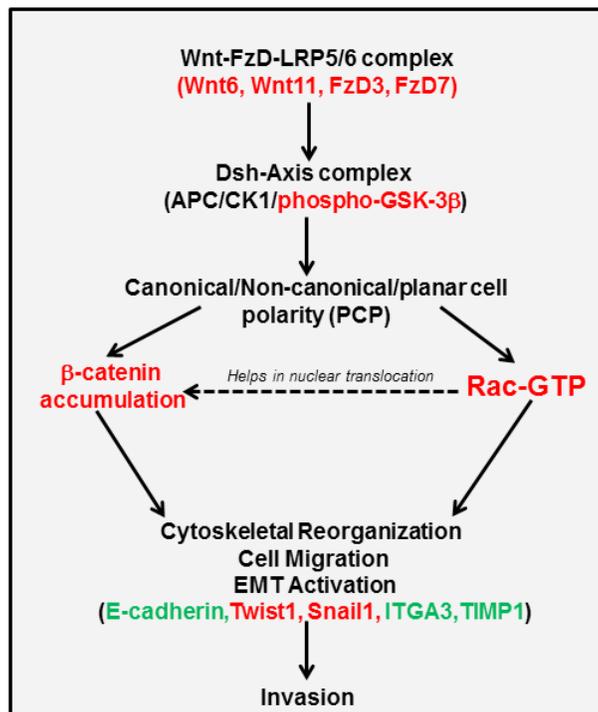
Faculty Mentor
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RIO KINASE 3 OVER EXPRESSION PROMOTES HEPATOCELLULAR CARCINOMA INVASION THROUGH INDUCTION OF EPITHELIAL MESENCHYMAL TRANSITION AND A POTENTIAL LINK TO WNT/ β -CATENIN PATHWAY ACTIVATION

Das T, Hassan S, Feng Q, Gretch D, Reyes J, Perkins J

Background: Recurrence is a major cause of mortality for patients with hepatocellular carcinoma (HCC) following liver transplantation. The presence of macroinvasion in the explanted liver is a significant predictor of recurrence, yet the mechanisms behind HCC macroinvasion, and thus, recurrence, remain ill-characterized. We previously identified RIOK3 as a prominently expressed gene in HCC tumors that recurred following transplantation. This is consistent with findings of increased RIOK3 expression in metastatic head, neck, and pancreatic cancers, which suggests RIOK3 is involved in cancer recurrence. In this study, we aimed to determine the pathway leading to HCC tumor invasion induced by RIOK3.



Methods: Ectopic RIOK3 expression was created by introducing a RIOK3 expression plasmid construct in HepG2 cell line. We studied EMT related markers, E-cadherin, Snail1, and Twist1 by Western blot and immunofluorescence analysis. Cell proliferation was measured by MTT assay, and cell migration was measured by in vitro wound healing assay. Activation of Rac1 and WNT/ β -catenin pathway was analyzed by western blot and quantitative PCR assays.

Results: We demonstrated that RIOK3 transformed the epithelial HCC cell line, HepG2, into a mesenchymal phenotype via EMT induction which induces invasion. When transfected into HepG2 cells, RIOK3 overexpression promotes activation of the small G protein Rac1 (GTP bound Rac) and activation of Wnt/ β -catenin signaling at multiple levels, including upregulation of Wnt6, Wnt11, FzD3 and FzD7 transcription, stabilization of β -catenin via GSK-3 β phosphorylation, and activation of WNT/ β -catenin transcriptional activity compared to control cells. We also determined that RIOK3 suppressed E-cadherin expression and induced Snail1 and Twist1 expression. Additionally, decreased expression of ITGA3 and

TIMP1 in RIOK3-overexpressing HepG2 cells correlated with metastasis-promoting, cell-specific morphological changes and increased cellular invasiveness.

Conclusions: These findings suggest that RIOK3 influences HCC cell motility through regulation of EMT-associated genes and in cooperation with activated Rac1 and WNT/ β -catenin signaling pathway activation.



Lacey N. LaGrone, MD, MA

Research Resident

Faculty Mentor

Charles N. Mock, MD, PhD, MPH

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Research Interests: Trauma quality improvement, implementation science

A SYSTEMATIC REVIEW OF GLOBAL IMPLEMENTATION OF THE WORLD HEALTH ORGANIZATION'S TRAUMA CARE GUIDELINES

LaGrone LN, Riggle KM, Joshipura MK, Quansah R, Reynolds T, Mock CN

Objective: Between 2004 and 2010, the World Health Organization (WHO), as part of the Essential Trauma Care Project, released four publications intended to provide guidance to policy-makers in low- and middle-income countries towards improvement in trauma care. We sought to understand the degree to which these guidelines have been implemented globally, including understanding location and type of implementation. By so doing, we hoped to identify areas needing improvement.

Methods: We conducted a systematic review in which the titles of the WHO trauma care guidelines were used as the search terms: "The Guidelines for Essential Trauma Care", "Prehospital Trauma Care Systems", "Guidelines for Trauma Quality Improvement Programmes". Nineteen databases were queried, validation of results was performed through citation analysis and expert consultation. Two reviewers independently scored sources.

Results: The above search returned 674 sources for inclusion. 474 referenced the publications merely as a source of information re: trauma care statistics and principles, 90 consisted of authors recommending use of the publications, and 110 sources described 138 implementation events. Among the sources which described implementation, the largest portion described needs assessments (44%), fewer described recommendation by stakeholders (28%), and the remainder described educational interventions (14%) or policy development (14%). The implementation of the publications was reported in 51 different countries, in addition to more broadly defined regions.

Table. Examples of implementation of each WHO Essential Trauma Care Project Publication

	Needs Assessment	Stakeholder	Policy	Education
Essential	Audit of trauma equipment and facilities at the national and each district referral hospital in East Timor, followed by feedback and recommendations to hospital staff.	Nationwide meeting with the College of Surgeons of Sri Lanka, Sri Lanka Medical Association, Ministry of Health, WHO country office, and non-governmental organizations in which guidelines were adapted to local context.	Guidelines referenced, and incorporated into, national standards for trauma care in Mexico.	Guidelines incorporated into curriculum, or listed as required reading, for online courses in Nigeria, Burkina Faso, Liberia, and China, for medical students, residents, and nurses.
Prehospital	Questionnaire developed based on guidelines used to assess availability and quality of prehospital care on Pakistani interurban roads.	The African Federation for Emergency Medicine Out-of-Hospital Emergency Care Workgroup Consensus Paper "strongly urges" use of guidelines in development of prehospital trauma care systems.	Guidelines incorporated into Colombian National Legislation: "Decrees and Resolutions" which defines basic qualifications for providers, ambulance equipment, and methods for audit.	Lay first-responder course on prehospital trauma care conducted in Kampala, Uganda, based in part on recommendations in guidelines.
QI	Guidelines used to assess trauma care and quality improvement in rural health district in South Africa.	Secretary of Neurotrauma Society of India makes explicit call for implementation of quality improvement programmes in quarterly newsletter, drawn from guidelines.	Preventable death panel instituted at tertiary-care teaching hospital in Ghana based on recommendations in Guidelines.	WHO/IATSIC* created a set of instructional materials, freely available online, for 2-3 day courses. In 2012 alone collaborators conducted courses in: Kenya, Liberia, Paraguay, Brazil, Malaysia, Thailand.

*International Association for Trauma Surgery and Intensive Care

Conclusions: The WHO trauma care guidelines have been widely implemented, in a variety of ways, including documentation of well over 100 events in more than 50 countries. However, given the substantial disparities that remain in trauma care, efforts to bring the standards described in the publications to the remaining 143 WHO member states are essential.



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SURGEON BEHAVIOR AFTER ANASTOMOTIC LEAK IN COLON SURGERY

Simianu VV, Basu A, Alfonso-Cristancho R, Flaxman AD, Flum DR

Background: Breakdown of a colorectal anastomosis is a rare but potentially life-threatening complication. Pressure testing the anastomosis (leak testing) can identify leaks intra-operatively and reduces the risk of leaks after surgery by up to 50%. Surgeons have varying opinions about the value of leak testing, and perceived value drives behavior. We evaluated the impact of having a surgical leak on a surgeons' leak-testing behavior during subsequent cases, to test the hypothesis that a recent leak would influence the perceived value of leak testing.

Methods: A prospectively gathered cohort from the Surgical Care and Outcome Assessment Program (SCOAP) in Washington State was used to quantify leak testing during elective colorectal procedures with testable anastomoses (left colectomy, low anterior resection, and total abdominal colectomy) and adverse events related to leak. We describe patterns of leak testing and leaks, stratified by surgeon volume. Higher volume surgeons were defined as performing 5 or more procedures per year. To test the hypothesis of behavior change, we explored a difference-in-difference non-parametric model to compare leak testing before and after a leak.

Results: From 2008 to 2013, surgeons performed 7,497 elective colorectal operations across 46 hospitals, with a leak rate of 2.6% (n=195). Higher-volume surgeons accounted for 83.2% of the cases (n= 6,234) in the time period. Mean leak testing rate for all surgeons was 85.9%. While leaks occur more often in untested cases (3.5% vs 2.5%, p=0.05), leak events and leak testing were not different between lower- and higher-volume surgeons. The overall rate of leak testing increased for both lower-volume (76 to 88%, p=0.007) and higher-volume (82 to 88%, p=0.002) surgeons over the study. Lower-volume surgeons seem to increase their testing after a leak, as shown in Table 1. However, our difference-in-difference analytic model was limited by small sample size at the individual surgeon level.

Conclusions: Intraoperative leak testing appears to increase the most for lower-volume surgeons who experienced a leak, suggesting that these surgeons may attribute higher value to leak testing after a leak. For higher-volume surgeons, it may be that surgeon-specific preferences and practice style are more influential in the uptake of leak testing rather than exposure to adverse events. These insights may help in crafting quality improvement initiatives around colorectal surgery that require clinician behavior change.

Table 1. Leak testing patterns before and after anastomotic leak.

Surgeon Volume	Test	Leak	No. of cases (% of all leaks)	Clustered by Surgeon	
				% leak testing (6 months before)	% leak testing (6 months after)
< 5 cases per year	No	Yes	9 (5%)	40%	50%
	Yes	Yes	30 (15%)	72%	100%
5+ cases per year	No	Yes	28 (14%)	73%	69%
	Yes	Yes	128 (66%)	88%	86%



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Research Interests: Cigarette smoke and microRNAs in esophageal cancer

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LYSYL-LIKE OXIDASE 2 (LOXL2) IS AN ONCOGENIC DRIVER OF MALIGNANCY REGULATED BY MIR-145 IN TOBACCO-ASSOCIATED ESOPHAGEAL ADENOCARCINOMA

Oyetunji SO, Xi S, Straughan D, Azoury S, Hong JA, Zhang M, Schrupp DS

Background: Although recently implicated in the pathogenesis of esophageal adenocarcinomas (EAC), the mechanisms by which cigarette smoke mediates initiation and progression of these malignancies have not been fully elucidated. In this study, a novel in-vitro model system was used to examine the effects of cigarette smoke on microRNA (miR) expression during tobacco-induced esophageal adenocarcinogenesis.

Methods: Immortalized esophageal squamous and Barrett's epithelia (Het-1A; CP-A, CP-C, respectively), and EAC lines (NCI-EsC1, NCI-EsC2, NCI-EsC3, OE-19, and OE-33) were cultured with or without cigarette smoke condensate (CSC) under relevant exposure conditions. Micro-array and qRT-PCR techniques were used to identify miRs consistently modulated by CSC in cell lines, with correlative analysis of EAC specimens/paired normal esophageal tissues. RNA crosslink immunoprecipitation, luciferase reporter assays, MTS, and xenograft experiments were performed to identify targets and characterize phenotypic effects of differentially expressed miRs.

Results: Sixty miRs were significantly induced, whereas twenty-one were repressed following 5-day CSC exposure. Sixteen of the induced miRs are oncomirs, including miR-21 and miR-372, which have been previously shown to be up regulated in esophageal cancers. Fourteen of the repressed miRs are tumor suppressors, including miR-487b and miR-217, which are epigenetically repressed in lung and esophageal cancers and silenced in normal respiratory and esophageal epithelia by cigarette smoke. miR-145, previously shown to be repressed in esophageal squamous cell cancers, was down-regulated in immortalized esophageal squamous and Barrett's epithelia, and EAC lines by CSC in a time and dose dependent manner. Endogenous levels of miR-145 were significantly lower in EAC lines/primary tumors compared to immortalized cells/normal mucosa ($p < 0.003$). Lysyl-like oxidase 2 (LOXL2), an oncogene not previously implicated in EAC, was identified as a novel, direct target of miR-145. CSC mediated repression of miR-145 coincided with up-regulation of LOXL2 expression in immortalized esophageal epithelia and EAC cells. Furthermore, repression of miR-145 coincided with over-expression of LOXL2 in EAC specimens, particularly those from smokers. Over-expression of LOXL2 significantly enhanced proliferation, invasion and migration of EAC in-vitro, and significantly increased tumorigenicity of EAC in athymic nude mice ($p = 0.006$); these findings were recapitulated with stable knockdown of miR-145 in EAC cells ($p = 0.011$).

Conclusions: Repression of miR-145 up-regulates a novel oncogenic driver of malignancy during tobacco-associated esophageal adenocarcinogenesis. These findings warrant further efforts to target aberrant LOXL-2 expression by reactivation of miR-145, or direct inhibition of LOXL2 expression or activity for treatment of EAC.



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Saman Arbabi, MD, MPH

ACUTE REHABILITATION AFTER TRAUMA: DOES IT MAKE A DIFFERENCE?

Nehra DN, Nixon Z, Lengenfelder C, Bulger EM, Arbabi S

Background: Following a traumatic injury patients and family members universally desire recovery of functional independence to enable safe discharge to home. This is a goal that is oftentimes not realized during the acute inpatient hospitalization, but rather, requires ongoing rehabilitation following discharge. The specific goals of this study were: 1) to describe the characteristics and immediate outcomes of trauma patients who received inpatient rehabilitation services, and 2) to determine the likelihood of eventual discharge home and the likelihood of death within 1-year for trauma patients who received inpatient rehabilitation as compared to a control group of propensity score-matched patients who did not receive inpatient rehabilitation.

Methods: Rehabilitation data for all patients discharged to a rehabilitation center following an acute trauma was collected from all rehabilitation centers in the state of Washington for two years (2011 and 2012). This unique state-wide rehabilitation data includes cognitive and motor skill scores before and after therapy. These charts were linked to the Washington State Trauma Registry (WTR), which contains patient and injury specific data, and the State of Washington Comprehensive Hospital Abstract Reporting System (CHARS) database, which contains mortality data. Propensity score matching was used to identify a control group of patients who were not discharged to a rehabilitation center and multivariate regression analysis was utilized to determine factors associated with the likelihood of discharge to home and 1-year mortality.

Results: Nine hundred and ninety-three trauma patients discharged to one of the 14 acute rehabilitation centers in the state of Washington between 2011-2012 were included in the study. The mean age of patients who received acute rehabilitation was 50.5 ± 23.5 years and there was a male predominance (68.3%). Almost all patients discharged to rehabilitation centers had either commercial or government-sponsored insurance with only 61 patients (6.1%) having no insurance. Most patients had suffered a blunt trauma (94.9%) with penetrating trauma accounting for 4.1% of all patients. The most common injury was a traumatic brain injury (TBI) with 34.2% of patients sustaining an isolated TBI and another 25.7% suffering a TBI in conjunction with either a spinal cord injury or major thoracic, abdominal or orthopedic injury. Most patients had an intermediate to high injury severity score (ISS) with 53.9% having an ISS between 9-24 and another 36.0% having an ISS of >25. The functional independence measure (FIM) scores at admission to and discharge from rehabilitation were used to determine improvement in functional status. Total FIM scores improved by 29 ± 17.0 points from 63.7 ± 20.3 to 92.2 ± 20.9 ($p < 0.0001$) with the majority of this improvement occurring in the motor category (mean Δ motor FIM 24.6 ± 14.6 , $p < 0.0001$) as compared to the cognitive category (mean Δ cognitive FIM 4.6 ± 5.7 , $p < 0.0001$). The vast majority of patients (78.2%) admitted to an acute rehabilitation center following trauma were successfully discharged to home. When patients discharged to a rehabilitation center were compared to a cohort of propensity score-matched control patients not discharged to a rehabilitation center, rehabilitation was found to significantly increase the likelihood of discharge to home for all age groups [OR 8.66, 95% CI 5.2-13.5] and decrease the 1-year mortality [OR 0.50, 95% CI 0.32-0.76].

Conclusions: Patients discharged to a rehabilitation center following an acute trauma experience a significant improvement in FIM scores and are more likely to be safely discharged home compared to those who do not receive rehabilitation. Our data suggests that acute trauma patients should be recognized as a population that enjoys marked benefit with inpatient rehabilitation services.



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Research Interests: Critical care, nutrition, metabolomics, trauma, pediatric surgery

Faculty Mentor

Grant E. O'Keefe, MD, MPH

A NOVEL DIAGNOSTIC AND PROGNOSTIC TOOL IN CRITICALLY-ILL TRAUMA PATIENTS: METABOLOMIC PROFILING REVEALS PERVASIVE CHANGES

Parent B, Aarabi S, Raftery D, O'Keefe GE

Background: Metabolomics is the study of metabolites within an organism and provides an elegant real-time summary of physiologic state. The metabolic profile is the sum of several hundreds of lipids, amino-acids, nitrates, and sugars which represent the ultimate downstream products of the genome and its interaction with the environment. By analyzing patients' serum and urine samples, prior studies have identified metabolic markers which have led to earlier identification of common illnesses like sepsis, acute respiratory distress syndrome, pneumonia, and cancer. However, these markers are not yet well-validated and large knowledge gaps exist. Further research in metabolomics may be especially relevant in trauma care, given that our current laboratory repertoire to identify and trend metabolic derangement can be both overly simplistic and misleading. This is particularly true in both shock and malnutrition states, where the utility of lactate, base deficit, and albumin has been repeatedly called into question. Metabolomics represents a potential new diagnostic and predictive tool that would allow for a more personalized and nuanced approach to trauma care.

Methods: Patients were included in the study if they were within 12 hours of blunt trauma and had either a systolic blood pressure of <90 mmHg or a base deficit >6 within the first hour of arrival. Serum and urine samples were obtained on hospital day 1, 3, 7, and 9. Patient charts were reviewed for clinical data. Healthy age and gender-matched volunteers donated samples in a fasting state at two time points separated by 72 hours. Samples from patients and controls were then analyzed using nuclear magnetic resonance (NMR) and mass spectrometry (MS). Partial least-squares discriminant-analysis models were applied to samples for comparison. Univariate and multivariate statistical analyses were used to select potential biomarkers of interest.

Results: 30 samples from 5 patients revealed pervasive changes in metabolic profiles. Specific changes in trauma patients seen on NMR (Fig 1a, b) include evidence of an impaired TCA cycle (elevated acetate, lactate, decreased citrate) and evidence of muscle catabolism (elevated tyrosine, phenylalanine, decreased hippuric acid). Similar pathway changes were seen in patient serum on LC-MS. Moreover, ongoing critical illness was associated with ongoing abnormalities in the metabolome.

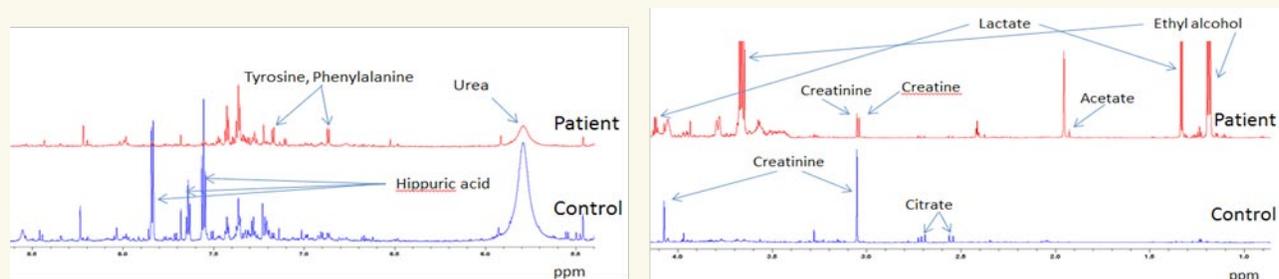


Fig 1a, b. Urine NMR spectra from trauma patients vs. control plotted with the same vertical scale for direct comparison of peak intensities.

Conclusions: Critically-ill trauma patients have an underlying inflammatory and catabolic burden which is demonstrable on metabolomics. Profiling the metabolome of a trauma patient and trending changes in specific metabolites over time allows for a more direct assessment of disease severity and tracks treatment efficacy. This technique represents a novel, rapid, and personalized diagnostic tool which has the potential to provide new therapeutic targets in trauma patients.



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Kimberly J. Riehle, MD

ENHANCED CYCLIC-AMP STIMULATED PROTEIN KINASE A ACTIVITY IN FIBROLAMELLAR HEPATOCELLULAR CARCINOMA

Riggle KM, Kazami M, Kenerson HL, Bauer R, Riehle KJ, Yeung RS

Background: Fibrolamellar hepatocellular carcinoma (FL-HCC) is a subtype of HCC that occurs in children and young adults without liver disease, and for which there are no effective non-surgical therapies. Genomic analysis identified a consistent mutation in FL-HCC leading to fusion of a heat shock protein (DNAJB1) and the catalytic subunit of protein kinase A (PRKACA). We sought to characterize this chimeric protein and its effects on protein kinase A (PKA) activity in human FL-HCC.

Methods: Gene and protein expression levels of PKA holoenzyme subunits in FL-HCCs, paired normal livers, 'classic' HCCs, and cholangiocarcinomas (CCs) were assessed by qPCR and immunoblotting. Subcellular localization of catalytic (C) and regulatory (R) subunits in FL-HCC and normal liver was determined by co-immunofluorescence and subcellular fractionation. Catalytic activity of PKA was measured by a radioactive kinase assay.

Results: The mutant transcript and protein were detected in all FL-HCCs, but not in normal liver, 'classic' HCC, and CCs. In FL-HCCs, the mutant transcript was expressed 10-fold higher than that of wild type PRKACA. (p -value 0.001). In normal liver, both C and R subunits localize to the cytoplasm, while in FL-HCCs the C subunit is also detected in the nucleus. cAMP-stimulated PKA activity was significantly higher in FL-HCCs compared to paired normal livers, while basal activities did not differ.

Conclusions: The DNAJB1-PRKACA fusion product is uniquely expressed in FL-HCC. cAMP-stimulated PKA activity is higher in FL-HCC compared to normal liver, possibly secondary to higher gene expression or abnormal subcellular location. This aberrant localization and enhanced activity may contribute to tumorigenesis in FL-HCC.



Morgan K. Richards, MD

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Medical School: Case Western Reserve University

Research Interests: Pediatric surgery outcomes research

Faculty Mentor

Adam B. Goldin, MD, MPH

ENDOSCOPIC, LAPAROSCOPIC, IMAGE-GUIDED PEDIATRIC GASTROSTOMY TUBE PLACEMENT: IMPROVED OUTCOMES WITH A STANDARDIZED APPROACH

Richards MK, McAteer JP, Shaw DW, Wahbeh GT, Foti JL, Melzer L, BA, Goldin AB

Background: Relatively recent medical advances such as percutaneous endoscopic (PEG), image-guided, laparoscopic and even robotic gastrostomy tube (GT) placement have become common among pediatric patients. These minimally invasive approaches may be quick to perform and simple to complete, but they are not without subsequent complications such as infection, leakage, device malfunction, dislodgement, hemorrhage and intra-abdominal organ injury. In addition, many of the procedures require planned interventions such as tube exchanges or conversions from gastrostomy to gastrojejunostomy. We hypothesized that implementation of a hospital-wide clinical standardized work (CSW) feeding tube pathway would be associated with a reduction in hospital resource utilization.

Methods: We performed a retrospective cohort study comparing all children undergoing GT or gastrojejunostomy tube (GJ) placement following implementation of the hospital-wide clinical standardized work (CSW) from June 1, 2013 - July 31, 2014 to those placed in a previous time period (January 1, 2010 - December 31, 2011). We limited follow up time to 365 days in both groups. Our primary outcome was the change in the rate of hospital resource utilization, defined as 1) GT/GJ-related emergency department visits, 2) planned events, or 3) unplanned events before and after implementation using adjusted Poisson regression. We also compared the time to first event between cohorts using adjusted Cox regression to understand the relative number of children requiring repeat utilization ($p < 0.05$). Adjustment factors included age, ASA class, gender, insurance, race, comorbidities and GT/GJ at initial placement.

Results: Prior to CSW implementation, 145 (48.7%) devices were placed surgically, 113 (37.9%) endoscopically, and 40 (13.4%) with an image-guided technique. After implementation, 105 (73.4%) were placed surgically, 23 (16.1%) endoscopically, and 15 (10.5%) with an image-guided technique. Prior to implementation, 174/298 (58.4%) patients required additional hospital utilization compared to 58/143 (40.6%) after implementation. Poisson regression demonstrated that following implementation, the rate of resource utilization decreased by over 50% (Incidence Rate Ratio: 0.47; 95%CI 0.37-0.60; $p < 0.001$). The risk of at least one additional feeding tube related intervention or emergency department visit was reduced by over 30% based on Cox regression (Hazard Ratio: 0.64; 95%CI 0.46-0.87; $p = 0.005$). This demonstrated that fewer children required at least one repeat GT/GJ-related hospital utilization event after algorithm implementation.

Conclusions: Care of this complex and heterogeneous patient population is currently spread among multiple providers and specialties leading to variability in the pre-operative workup, intra-operative technique, and post operative care. Our study shows an association between a standardized approach to GT/GJ placement and decreased hospital resource utilization.



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Research Interests: Decision making in healthcare

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ALVIMOPAN USE, OUTCOMES, AND COSTS: A REPORT FROM THE SCOAP CERTAIN COLLABORATIVE

Pugel AE, Simianu VV, Davidson GH, Fichera A, Flum DR, Farjah F

Background: Alvimopan is a mu-opioid antagonist believed to prevent narcotic-mediated ileus. Randomized clinical trials show that alvimopan use in colorectal patients leads to shorter length of stay (LOS). However, its adoption into routine clinical practice, as well as its effectiveness, have not been well characterized. The cost of alvimopan may be one barrier to wider use of this drug. We aimed to describe the use of alvimopan across hospitals in Washington (WA) State, and to compare LOS and costs between patients who did and did not receive the drug.

Methods: A cohort study was conducted of patients undergoing elective colorectal surgery between 2009 and 2011 at participating hospitals from the Surgical Care and Outcomes Assessment Program (SCOAP). SCOAP data was linked to data from the WA State Comprehensive Hospital Abstract Reporting System (CHARS) to determine charges. A payer-perspective analysis was performed based on costs estimated using cost-to-charge ratios and adjusted for inflation. Generalized estimating equations and jackknife variance estimators were used to compare LOS and costs after adjusting for demographic variables, comorbid conditions, operative indications and characteristics, process-of-care measures, and clustering at the hospital-level.

Results: Over three years, 8,129 patients underwent colorectal surgery across 46 hospitals. Eighteen hospitals administered alvimopan at least once. Among 4,665 patients cared for at alvimopan hospitals, 729 (16%) received the drug. At alvimopan hospitals, patients who received alvimopan were more likely to have commercial insurance (78% versus 71%, $p=0.001$), have no comorbid conditions (76% versus 69%, $p=0.001$), have a malignancy as their indication for surgery (54% versus 43%, $p<0.001$), and undergo a laparoscopic approach (58% versus 41%, $p<0.001$). The unadjusted median LOS was significantly lower for patients who received alvimopan compared to those who did not (4 versus 5 days, $p<0.001$), as were unadjusted median costs (\$7,135 versus \$7,409, $p=0.036$). After adjustment, LOS was ~18 hours shorter (-0.8 days, 95% CI -1.1 to -0.5 days), and hospital costs were significantly lower (-\$1050, 95% CI -\$1455 to -\$646) among those receiving alvimopan.

Conclusions: Alvimopan was associated with a decrease in LOS of less than one day, as well as a decrease in hospital costs. Effectiveness evaluations are important in determining the value of drugs and devices prior to routine adoption.

POSTER ABSTRACTS

IN
PRESENTATION
ORDER

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DIFFERENTIAL REGENERATIVE CAPACITY OF NEONATAL MOUSE HEARTS AFTER CRYOINJURIES

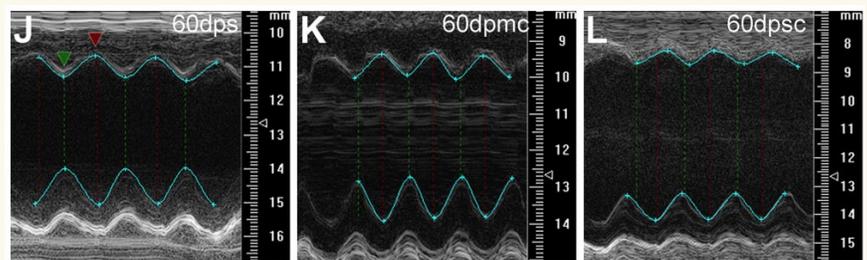
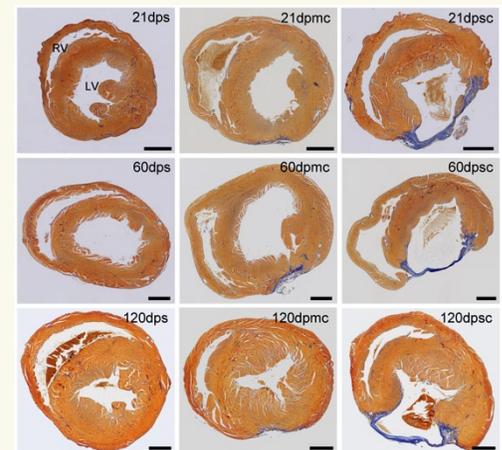
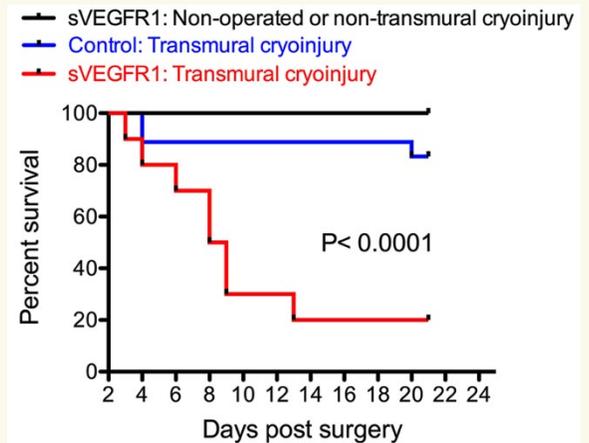
Darehzereshki A, Rubin N, Fraser J, Osorio A, Warburton D, Kaartinen V, Lien CL

Background: Mammalian adult hearts cannot regenerate in response to tissue damage. Interestingly, neonatal mouse hearts have regenerative capacity after ventricular resection. Cryoinjury is thought to be more similar to damages caused by myocardial infarction than resection. To determine if neonatal mouse hearts can regenerate after cryoinjury and how transmural affects the regenerative responses, we developed injury models to produce transmural (severe) and non-transmural (mild) injuries to the hearts.

Methods: A 2 mm metal probe was chilled in liquid nitrogen for 30 seconds. Non-transmural and transmural cryoinjuries were created by application of the pre-chilled probe on the left ventricular anterolateral wall for 1 and 5 seconds, respectively. Functional and tissue studies were done at 21, 60 and 120 days after surgery.

Results: In contrast to ventricular resection, neonatal mouse hearts fail to regenerate and show severe impairment of cardiac function at 21, 60 and 120 days post transmural (severe) cryoinjury. Minimal scar tissue remains after non-transmural (mild) cryoinjury. Epicardial activation and new coronary vessel formation occur after cryoinjury. However, we did not observe increased cardiomyocyte proliferation after transmural cryoinjury; this is consistent with the finding that neonatal mouse hearts regenerate by cardiomyocyte proliferation after ventricular resection. When neovascularization is blocked by a VEGF-sequestering soluble receptor (sVEGFR1), neonatal mouse hearts cannot survive transmural cryoinjury.

Conclusions: Neonatal mouse hearts do not regenerate after transmural cryoinjury due to the failure of cardiomyocytes to undergo proliferation. Neovascularization is essential for survival of neonatal mice after transmural cryoinjury.





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Nicole S. Gibran, MD

HOSPITAL-ACQUIRED COMPLICATIONS ALTER QUALITY OF LIFE IN BURN SURVIVORS

Deeter LA, Seaton M, Carrougher GJ, McMullen K, Pham TN, Mandell SP, Gibran NS

Background: Successful burn care should help individuals to achieve functional recovery after an injury. Studies have correlated hospital-acquired complications (HACs) with poor long-term outcomes in some populations. The purpose of this study is to determine whether HACs alter patient-reported quality of life in adult burn survivors.

Methods: We followed 496 adults with major burn injury longitudinally as part of a burn outcomes study (1993-2014). Study participants completed SF-12® Health surveys providing mental (MCS) and physical (PCS) component summary scores at discharge, 6-, 12- and 24-months following injury. We reviewed inpatient medical records for complications during the acute care of a thermal injury. Complications were identified using discharge summary and chart ICD-9 codes. We used descriptive statistics to compare demographic and injury characteristics. Stepwise linear regression analyses determined the impact of significant variables on longitudinal MCS and PCS scores. Burn and graft TBSA, age, and gender were included as predictor variables in univariate models and added to multivariate models when they were significant.

Results: Table 1 summarizes population characteristics. Multivariate regression statistics evaluated significant complication groups and biographical variables. UTI, VTE, pulmonary complications, renal failure, and cardiogenic shock significantly influenced PCS scores.

Conclusions: We confirm that inpatient complications impact long-term patient reports of quality of life especially PCS scores. Gender and age related changes over time are consistent with prior findings. Our data confirm the need to consider the influence of hospital acquired complications on patient reported long-term outcomes and support national efforts to reduce complications in burn patients.

Table 1.

Age: Mean (SD)	43.8 (15.4), 18-91
% Male (n)	74.4% (369)
% TBSA burned: Median (IQR), range	14.9% (6-28), 0.3-70
% TBSA grafted: Median (IQR), range	5.3% (1.6-14.2), 0-88.7
# Operations: Mean (SD)	2.6 (0-19)
% With pre-burn co-morbidities: (n)	26.8% (133)
% Inhalation injury: (n)	11.9% (59)
# Days on ventilator (n=145): Mean (SD), range	13.1 (15.1), 1-75
% Working pre-burn: (n)	58.1 % (288)



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KNOCKOUT OF P27KIP1 ENHANCES ISCHEMIA INDUCED COLLATERALIZATION THROUGH A NOVEL COLLATERAL PATHWAY

Eliahoo G, Bates O, Tang GL

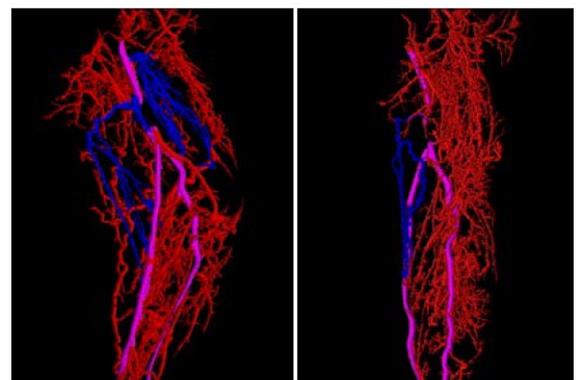
Objectives: The gene p27Kip1 (p27) affects human response to arterial injury. Overexpression of p27 inhibits vascular endothelial and smooth muscle cell (VSMC) proliferation and angiogenesis. We previously showed that p27^{-/-} mice reperfused more effectively than wildtype (wt) mice after hindlimb ischemia and that p27^{-/-} VSMC migrate more and cause increased gel contraction when compared to wt VSMC. To test the hypothesis that ischemic collateralization is enhanced by deficiency of p27 within arterial wall cells as opposed to within bone marrow derived cells, we performed in vivo experiments using p27 knockout (p27^{-/-}) and wild type (wt) mice. We also tested the effect of genetic dosage of p27 and matrix metalloproteinase inhibition on cell migration and gel contraction in vitro.

Methods: Hindlimb ischemia was induced by left femoral artery ligation in p27^{-/-} and wt (C57BL/6) female mice without and with reciprocal bone marrow transplantation (BMT). Mice were followed by weekly footpad laser Doppler perfusion imaging (LDPI) until sacrifice (day 28 for mice without BMT, day 14 for BMT mice). MicroCT scanning of both hindlimbs for all mice was performed after sacrifice. VSMC were isolated from p27^{-/-}, p27^{+/-}, and wt mice and used in migration and gel contraction assays in the absence and presence of the matrix metalloproteinase (MMP) inhibitor, BB94. MMP2 and MMP9 mRNA expression was measured by qRT-PCR.

Results: The gracilis collateral diameters were similar for the non-ischemic hindlimbs of the p27^{-/-} and wt mice, and this collateral pathway increased similarly in both genotypes after ischemia by microCT. However, the p27^{-/-} mice enlarged a novel collateral pathway significantly more than the wt mice (158 ± 18 vs 82 ± 22 μm, p < 0.001, Figure 1). The number of detected vessels increased in the p27^{-/-} ischemic hindlimb more than in the wt (86 ± 13 and 68 ± 5, p < .05). BMT experiments showed that the donor bone marrow genotype did not affect collateralization. The p27^{-/-} mice transplanted with wt bone marrow significantly enlarged their bridge collaterals by microCT, whereas it was difficult to identify the bridge collaterals in wt mice transplanted with p27^{-/-} bone marrow. In vitro studies showed that p27^{+/-} VSMC behaved similarly to wt VSMC in the migration and gel contraction assays. Migration and collagen gel contraction were abolished in both p27^{-/-} and wt cells in the presence of BB94, a nonspecific matrix metalloproteinase (MMP) inhibitor. p27^{-/-} cells expressed significantly more MMP2 mRNA than wt cells.

Conclusions: Knockout of p27 enhances arterial collateralization in response to hindlimb ischemia through enlargement of a new collateral pathway. The mechanism through which it affects collateralization is dependent on local arterial wall cells and not on bone marrow derived cells. The increased migration and collagen gel contraction seen in p27^{-/-} VSMC are likely due to increased expression of MMP2. Our results suggest that p27 affects collateralization through its role in regulating MMP2 expression in local arterial wall cells.

Figure 1.



P27^{-/-}

Wt



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LIVER TRANSPLANTATION OUTCOMES AMONG PATIENTS WITH INBORN ERRORS OF METABOLISM: WORTH THE RISK?

Flaster H, Dick A, Li M, Healey P, Hansen R, Montenovo M

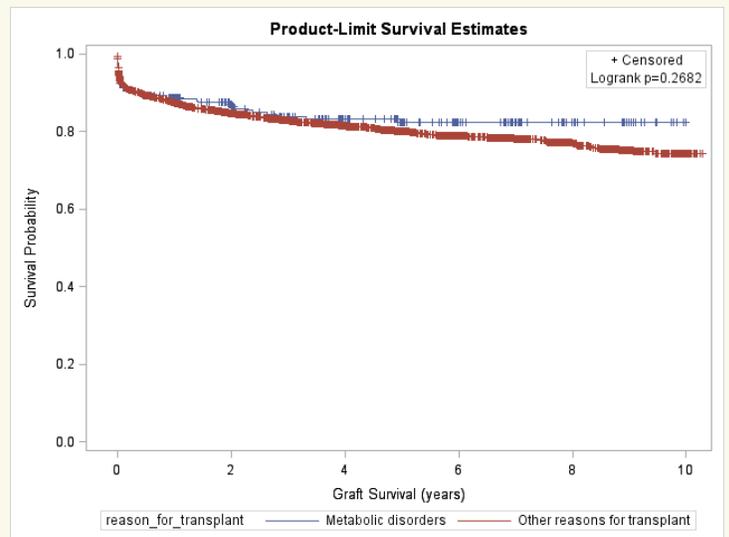
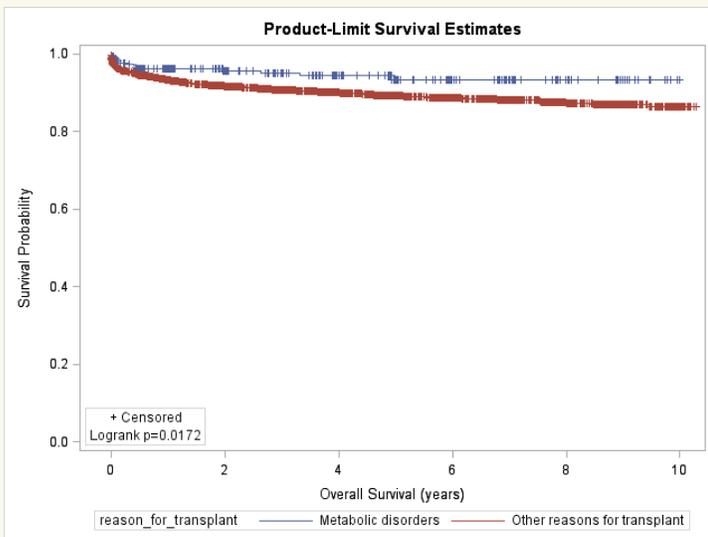
Background: Evidence is limited as to whether children with inborn errors of metabolism should undergo liver transplantation versus medical management. To answer this important question, we first sought to explore the differences in clinical outcomes between patients transplanted with and without metabolic disorders. Second, we estimated the economic impact associated with liver transplantation versus medical management.

Methods: We conducted a retrospective analysis using all single-organ first liver transplants of children under age 18 in the UNOS database from February 2002 through December 2012. Graft and patient survival were compared between children with and without metabolic disorders using the Kaplan-Meier estimator and multivariate Cox Proportional Hazards models. A Markov model was constructed using already published data to estimate the economic outcomes associated with liver transplantation versus medical management. Lifetime direct and indirect costs, life expectancies and quality-adjusted life-years (QALYs) were simulated for a hypothetical cohort of newborns with inborn errors of metabolism.

Results: There were 291 transplants for inborn errors of metabolism and 4,402 for other reasons. Survival analysis indicated similar patient and graft survival (Figure 1). Liver transplantation was the dominant therapeutic strategy, saving \$1,594,995 in lifetime societal costs and generating 8 more QALYs compared to nutritional support. Liver transplantation remained dominant from the payer perspective, saving \$1,171,978 throughout lifetime.

Conclusions: Children with inborn errors of metabolism have excellent patient and graft survival with transplantation. Liver transplantation appears to be a cost-effective therapy compared to medical management.

Figure 1. Kaplan-Meier plots for graft and overall survival.





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OUTCOMES OF KETOROLAC ADMINISTRATION IN MICROSURGICAL BREAST RECONSTRUCTION

Miranda SG, Gougoutas AJ, Gallagher T, Rivara A, Mathes DW

Background: Free flap loss in autologous breast reconstruction is a devastating complication. Intraoperative vascular complications have been shown to lead to higher rates of thrombosis and subsequent flap loss. The use of postoperative heparin may decrease rates of thrombosis and prevent flap failure. Ketorolac, with its known anticoagulant effects, has recently been shown to provide protective effects against the development of microvascular thrombosis in lower extremity free flaps. We hypothesize that the use of Ketorolac is safe in cases of free flap breast reconstruction complicated by intraoperative microvascular insult. Ketorolac may decrease rates of secondary thrombosis and flap loss in breast reconstruction.

Methods: A retrospective chart review was performed for identifying all patients who underwent autologous, free flap reconstruction at the University of Washington between the years of 2009–2013. Those cases with intraoperative vascular complications were categorized into one of two groups. Group A received intraoperative and postoperative Ketorolac +/- Heparin. Group B were patients who did not receive either. Rates of postoperative hematoma, acute renal failure, vascular thromboses and flap loss were compared.

Results: A total of 117 patients fulfilled inclusion criteria. Forty-nine patients received intraoperative and postoperative Ketorolac +/- Heparin (group A). Sixty-nine patients did not receive any intraoperative anticoagulant (group B). Group A had a 15% hematoma rate compared to a 16% rate in group B patients. Acute renal failure was 2% in group A and 0% in group B. Thrombus rates were 8% versus 15% for group A and B. Finally, flap loss was lower with a 4% rate in group A patients when compared to 10% in group B patients (Table 1).

Conclusions: Ketorolac administration in the setting of intraoperative microvascular insults, revealed that patients who received Ketorolac had an increased operative time and illustrated that patients who smoked or had a history of coagulation had a higher rate of administration. Ketorolac administration did not result in an increase rate of hematoma or acute renal failure, demonstrating its safety in microsurgical breast reconstruction. This may decrease rates of postoperative thrombosis and flap loss as a trend towards statistical significance was identified. Further studies with larger samples sizes, however, are required.

Table 1. Complications between Group A and B.

Complications	Group A Ketorolac (n=49)	Group B Non-Ketorolac & Non-Heparin (n=69)	p-value
Hematoma	8/49 (16%)	11/69 (16%)	0.199328
Acute Renal Failure	1/49 (2%)	0/69 (0%)	0.415254
Thrombus	4/49 (8%)	10/69 (15%)	0.138083
Flap Loss	2/49 (4%)	7/69 (10%)	0.141909



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LONG-TERM OUTCOMES OF RECTOSIGMOID NEOCOLPORRAPHY IN MALE-TO-FEMALE GENDER REASSIGNMENT SURGERY

Morrison SD, Satterwhite T, Grant DW, Laub Sr. DR, VanMaasdam J

Background: Favorable outcomes of rectosigmoid neocolporraphy have previously been reported. Unfortunately, rectosigmoid transfers are still perceived negatively, usually relegated to secondary vaginoplasties. This study aims to provide an objective investigation into the safety and efficacy of rectosigmoid neocolporraphy for primary vaginoplasty in the male-to-female (MtF) patient.

Methods: A retrospective review was performed on MtF patients who had undergone primary rectosigmoid neocolporraphy with the senior author. Patient data including demographics, medical history, complications, and the need for revisional surgery were obtained. Direct inquires were conducted to determine patients' level of satisfaction with appearance, sexual function, and ease of post-operative recovery.

Results: Eighty-three patients were included over the course of 22 years with an average clinical follow-up of 2.2 years (85 patients) and phone interview follow-up of 23 years (21 patients). Overall, the patients were healthy with minimal comorbidities. Forty-eight patients (58%) had complications, but the majority were minor and consisted mainly of stricture or excessive protrusion of the corpus spongiosum. Smoking was associated with higher complication rates, especially stricture formation. Excessive mucorrhea occurred in 28.6% of our cohort. Overall patient satisfaction with appearance and sexual function (among those who were sexually active) was high.

Conclusions: This study is one of the largest and longest reported series of rectosigmoid transfers for primary vaginoplasty. Advantages include long vault length, self-lubrication, a natural appearance, sensibility, and lack of malodor. Disadvantages include strictures or leaks of the intestinal anastomosis, and the need to enter the abdomen, which adds a layer of complexity to the procedure. Rectosigmoid neocolporraphies have many times been recommended for secondary or revisional surgery when other techniques, such as penile inversion, have failed. However, we believe the rectosigmoid transfer is safe and efficacious, and it should be offered to MTF patients for primary vaginoplasty.



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IMPROVEMENT IN PULMONARY FUNCTION FOLLOWING LAPAROSCOPIC GASTRIC BYPASS FOR PATIENTS WITH INTERSTITIAL LUNG DISEASE

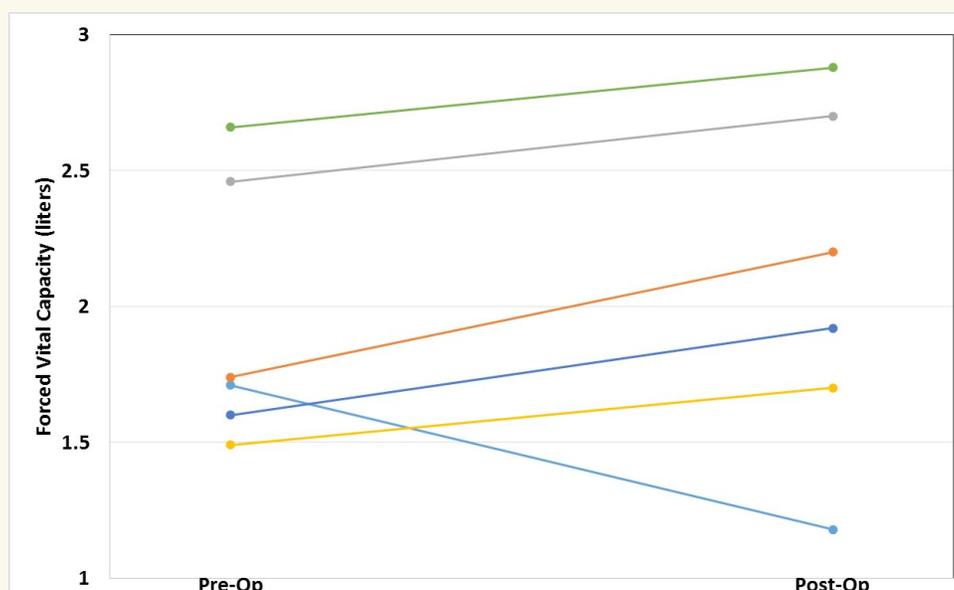
Mourot JM, Hinojosa MW, Pellegrini CA, Raghu G, Khandelwal S

Background: Morbidly obese patients with progressive interstitial lung disease (ILD) face two important challenges: preservation of lung function and candidacy for lung transplantation should the need arise. Roux-en-Y gastric bypass may improve pulmonary mechanics and slow pulmonary disease progression both by weight loss and reduction in gastroesophageal reflux and micro aspiration. We therefore sought to evaluate the safety and efficacy of gastric bypass in the morbidly obese patient with interstitial lung disease.

Methods: A multiyear retrospective review was performed looking at all bariatric referrals at the University of Washington Medical Center from January 2009 - December 2013 with a concurrent diagnosis of interstitial lung disease. Postoperative change in forced vital capacity was evaluated as a marker for progression of ILD.

Results: 6 patients with advanced stages of interstitial lung disease (mean age of 51, mean BMI of 47 and mean forced vital capacity of 57% predicted) underwent laparoscopic Roux-en-Y gastric bypass (5 patients) or laparoscopic sleeve gastrectomy (1 patient). All gastric bypass patients exhibited a post-operative increase in forced vital capacity; the only drop in forced vital capacity occurred in the patient who underwent sleeve gastrectomy. There were no perioperative complications and average hospital length of stay was 3 days.

Conclusions: Bariatric surgery in the morbidly obese patient with interstitial lung disease can be performed with minimal morbidity/mortality by a multidisciplinary care team with expertise in pulmonary medicine, ICU care, and bariatric surgery. In this study, all patients undergoing laparoscopic gastric bypass exhibited post-operative improvement in their forced vital capacity.





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RABBIT ANTITHYMOCYTE GLOBULIN IS ASSOCIATED WITH IMPROVED PATIENT AND GRAFT SURVIVAL IN LIVER TRANSPLANTATION. EXPERIENCE WITH 595 PATIENTS AT THE UNIVERSITY OF WASHINGTON

Pearson TR, Jalikis FG, Javed I, Li M, Yeh MM, Dick AA, Hansen RN, Reyes JD, Montenovo MI

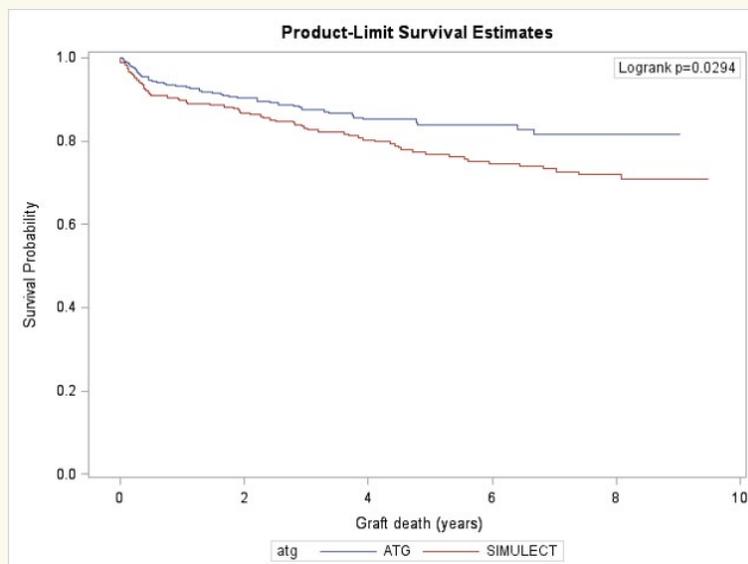
Background: The use of induction therapy in liver transplantation is debatable. The most common agents used include interleukin-2 receptor antibodies (IL-2R blockers) and rabbit anti-thymocyte globulin (r-ATG). No studies to date have compared the use of these agents in liver transplantation. We aimed to compare clinical outcomes of two induction protocols in liver transplant recipients.

Methods: We conducted a retrospective cohort analysis using the University of Washington Transplant Database from January 2005 through December 2012 for adult (≥ 18 year old) primary liver transplants performed at our institution. All patients received induction therapy with r-ATG or IL-2R blocker. Primary endpoints were patient and graft survival using Kaplan-Meier. Cox Proportional Hazards models were constructed to assess variables associated with both patient and graft survival.

Results: We identified 595 patients. 322 patients received r-ATG and 273 patients received IL-2R blocker. Demographic data is depicted in Table 1. Acute cellular rejection was higher with IL-2R blocker than with r-ATG group (27% vs 18% $p < 0.03$). Both patient and graft survival were superior with r-ATG than with IL-2R blocker at 1, 3 and 5 years. (Figure 1). Female recipient, MELD score and HCC were associated with less favorable patient and graft survival.

Conclusions: The use of r-ATG for induction therapy in liver transplantation is associated with lower rejection rate and improved patient and graft survival.

Figure 1. Graft Survival comparing r-ATG vs IL-2R inhibitor.





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CLINICAL PROFILING OF BCL-2 FAMILY MEMBERS IN THE SETTING OF BRAF INHIBITION OFFERS A RATIONALE FOR TARGETING DE NOVO RESISTANCE USING BH3 MIMETICS

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Background: While response rates to BRAF inhibitors (BRAFi) are high, disease progression emerges quickly. One strategy to delay the onset of resistance is to target anti-apoptotic proteins such as BCL-2, known to be associated with a poor prognosis.

Methods: We analyzed BCL-2 family member expression levels of 34 samples from 17 patients collected before and 10 to 14 days after treatment initiation with either vemurafenib or dabrafenib/trametinib combination. The observed changes in mRNA and protein levels with BRAFi treatment led us to hypothesize that combining BRAFi with a BCL-2 inhibitor (the BH3-mimetic navitoclax) would improve outcome. We tested this hypothesis in cell lines and in mice.

Results: Pretreatment mRNA levels of *BCL-2* negatively correlated with maximal tumor regression. Early increases in mRNA levels were seen in *BIM*, *BCL-XL*, *BID* and *BCL2-W*, as were decreases in *MCL-1* and *BCL2A*. No significant changes were observed with *BCL-2*. Using reverse phase protein array (RPPA), significant increases in protein levels were found in *BIM* and *BID*. No changes in mRNA or protein correlated with response. Concurrent BRAF (PLX4720) and BCL2 (navitoclax) inhibition synergistically reduced viability in BRAF mutant cell lines and correlated with down-modulation of *MCL-1* and *BIM* induction after PLX4720 treatment. In xenograft models, navitoclax enhanced the efficacy of PLX4720.

Conclusions: The combination of a selective BRAF inhibitor with a BH3-mimetic promises to be an important therapeutic strategy capable of enhancing the clinical efficacy of BRAF inhibition in many patients that might otherwise succumb quickly to *de novo* resistance.



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BURN WOUND INFECTIONS DO NOT INCREASE THE RISK OF HYPERTROPHIC SCARRING

Seaton ME, Sood RF, Carter DW, Honari S, Hocking AM, Gibran NS

Background: Hypertrophic scarring is a common late-complication of burn injuries that can cause severe functional impairment. The mechanism of hypertrophic scarring is incompletely understood but may be influenced by inflammation; infection may contribute to hypertrophic scarring by provoking an inflammatory response. The purpose of this study was to determine if burn wound infections increase the risk of hypertrophic scarring.

Methods: The prospectively enrolled sample included adults (age \geq 18) with burn size greater than 20% of total body surface area (TBSA) who were admitted to our burn center (2006 - 2013). Burn wound infection data was collected by chart review and ICD-9 codes. Vancouver Scar Scale (VSS) scores were determined at least 2.5 months after inpatient discharge. Hypertrophic scarring was defined as VSS \geq 8.

Results: There were 98 subjects included in the study. Seventy-nine (81%) of the subjects were male, the median age was 39 years (range 18-74 years), and the median TBSA was 30% (range 20-65%). Forty-two subjects (43%) developed a burn wound infection. Sixty-two (63%) developed a hypertrophic scar. Univariate analysis showed an association between wound infection and hypertrophic scarring (prevalence ratio (PR): 1.42; 95% CI: 1.05-1.92). However, Poisson multivariate analysis, which controlled for other variables thought to contribute to hypertrophic scarring, including %TBSA, number of burn operations, and race/ethnicity, does not support this association between wound infection and hypertrophic scar formation (PR: 1.20; 95% CI: 0.82-1.76).

Conclusions: Burn wound infections are not an independent risk factor for hypertrophic scarring when controlling for other factors associated with scarring. Other complications that typically correlate with wound infections, such as high %TBSA burn and multiple burn surgeries, may account for the hypertrophic scarring frequently observed in patients with wound infections.



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EVALUATING THE MECHANISMS OF IMPROVED GLUCOSE HOMEOSTASIS AFTER BARIATRIC SURGERY IN OSSABAW MINIATURE SWINE

Sham JG, Simianu VV, Wright AS, Stewart S, Alloosh M, Sturek M, Cummings DE, Flum DR

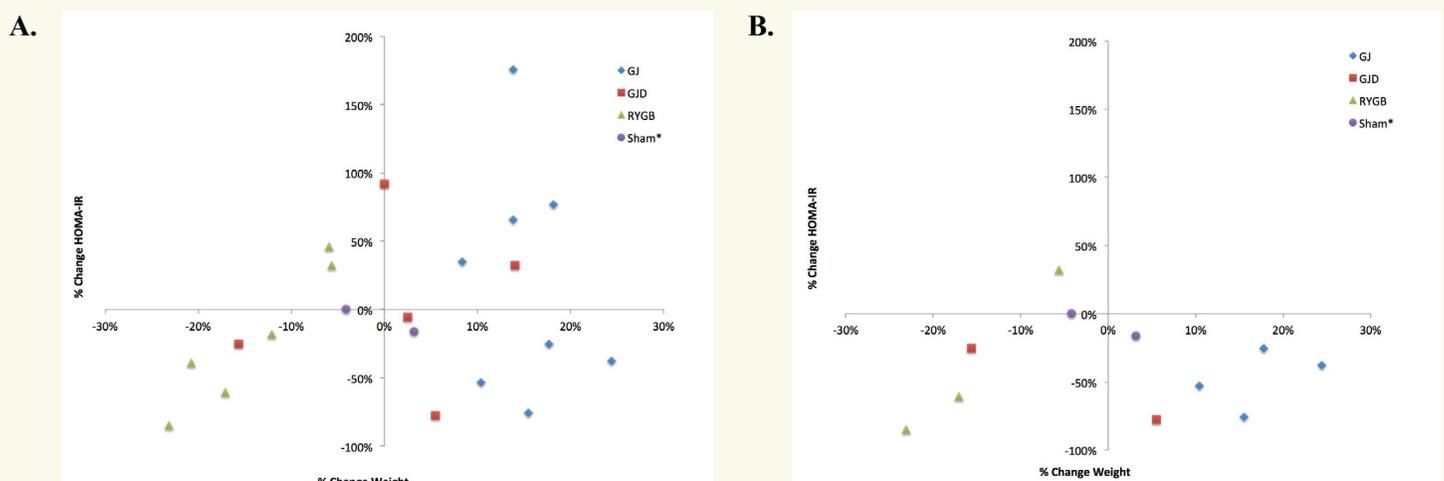
Background: Roux-en-Y gastric bypass (RYGB) is the most common bariatric operation; however, the mechanism underlying the profound weight-independent effects on glucose homeostasis remain unclear. Large-animal models of naturally occurring insulin resistance (IR), which have been lacking, would provide opportunities to elucidate such mechanisms. Ossabaw miniature swine naturally exhibit many features that may be useful in evaluating the anti-diabetic effects of bariatric surgery.

Methods: Glucose homeostasis was studied in 53 Ossabaw swine. Thirty-two received an obesogenic diet and were randomized to RYGB, gastrojejunostomy (GJ), gastrojejunostomy with duodenal exclusion (GJD), or sham operations. Intravenous glucose tolerance tests and standardized meal tolerance tests were performed prior to, 1, 2, and 8 weeks after surgery and at a single time-point for regular-diet control pigs.

Results: High-calorie-fed Ossabaws weighed more and had greater IR than regular-diet controls, though only 70% developed IR. All operations caused weight-loss-independent improvement in IR, though only in pigs with high baseline IR. Only RYGB induced weight loss and decreased IR in the majority of pigs, as well as increasing $AUC_{\text{insulin}}/AUC_{\text{glucose}}$.

Conclusions: Similar to humans, Ossabaw swine exhibit both obesity-dependent and independent IR. RYGB promoted weight loss, IR improvement, and increased $AUC_{\text{insulin}}/AUC_{\text{glucose}}$, compared to the smaller changes following GJ and GJD, suggesting a combination of upper and lower gut mechanisms in improving glucose homeostasis.

Figure 1. Change in body weight and HOMA-IR by operation at 8 weeks. A) Percent change in weight and HOMA-IR. B) Percent change in weight and HOMA-IR in pigs with above-median baseline HOMA-IRs.





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COMPLETION OF CLEFT CARE: A SINGLE SURGEON'S EXPERIENCE WITH UNILATERAL CLEFT LIP AND PALATE

Sousa JD, Tse R, Gruss JS

Background: One of the greatest challenges in plastic surgery is the management of cleft lip and palate from birth to adulthood. This comprehensive care begins shortly after birth and involves a large multidisciplinary team including plastic surgery, otolaryngology, oral surgery, orthodontics, dentistry, pediatrics, speech pathology, and social work. Although there is no internationally accepted protocol for the care of these patients, there is an ideal outcome shared among all providers involved in cleft care: normal appearance of the lip and nose, normal nasal airway, normal occlusion, normal speech, normal hearing, and appropriate psychosocial development. We aim to describe the long-term outcomes achieved at our center, specifically describing the surgical procedures required to bring a patient to completion of their cleft care.

Methods: All patients with unilateral cleft lip presenting to a single surgeon (JSG) between 1992 and 2012 were reviewed. Only patients who received the entirety of their care by the senior surgeon are included. Medical records were reviewed including operative reports, clinical notes, and serial photographs. Primary outcome was the aesthetic appearance of the lip and nose, evaluated using Asher-McDade scores. In addition, a subgroup of patients undergoing primary septoplasty at the time of initial cleft lip repair were evaluated using Asher-McDade scores, comparing them to those without primary septal repositioning at the initial operation.

Results: 226 patients with unilateral cleft lip with or without cleft palate presented for initial cleft care by the senior surgeon between 1992 and 2012. All patients born after 1998 were excluded, leaving 59 patients who reached at least 16 years of age at the time of data collection. 17 of these were lost to follow up before completion of their cleft care, and 11 are still undergoing treatment within our institution. 31 patients reached completion. All patients underwent primary cleft lip repair and primary rhinoplasty at age 3-6 months. Other surgical procedures required to bring patients to completion included: palatoplasty (n=18, 58.1%), tip rhinoplasty (n=7, 22.5%), alveolar bone graft (n=25, 80.6%), secondary rhinoplasty with cartilage grafting (n=17, 54.8%), LeFort 1 advancement (n=11, 35.4%), and speech surgery (n=9, 29.0%). Of note, in 2005 the senior surgeon began performing primary septoplasty on all patients undergoing initial repair. These patients (who have not yet reached completion) were included as a subgroup to compare outcomes with and without primary septoplasty. Asher-McDade scores demonstrated an average of "good" to "very good" aesthetic outcomes for all patients reaching completion. Comparison of patients with and without septorhinoplasty demonstrated an average of "good" to "very good" aesthetic outcomes for both groups.

Conclusions: Management of unilateral cleft lip and palate is a complicated and carefully orchestrated process beginning at birth and continuing into young adulthood. Our long-term outcomes demonstrate successful completion of treatment of a large number of patients, with exceptional outcomes, achieving the goals normal function and appearance of the cleft lip and nose.



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RISK FACTORS FOR BURN WOUND INFECTION: DATA FROM THE INFLAMMATION AND THE HOST RESPONSE TO INJURY STUDY

Thompson CM, O’Keefe GE, Gibran NS, Arnoldo BD, Gamelli RL, Herndon DN, Tompkins RG

Background: Burn wound infection is a serious complication following thermal injury that leads to significant morbidity, mortality and cost. Burn size is the main risk factor for burn wound infection. The Inflammation and the Host Response to Injury (“Glue Grant”) study is a multicenter research collaborative designed to advance our understanding of the host’s response to severe injury. We sought to identify risk factors for burn wound infection in this cohort.

Methods: We analyzed data from the burn injury subjects enrolled in the Glue Grant. Patient and injury characteristics were analyzed for association with burn wound infection using multivariate logistic regression analysis. We were specifically interested in factors including early blood transfusion and practice variations.

Results: There were 573 subjects with a mean age of 26; 72% were male. In addition to total body surface area, transfusion in the first 48 hours after injury and transfer to a burn center ≥ 24 hours after injury were independently associated with burn wound infection. Early transfusion increased the risk of burn wound infection by three-fold while delayed transfer increased the risk of burn wound infection by over five-fold.

Risk Factor for Burn Wound Infection	Odds Ratio	95% Confidence Interval	P-value
Transfusion in 1 st 48hrs	3.1	1.4-6.8	0.004
Transfer to burn center ≥ 24 hrs post-injury	5.5	2.1-14.6	0.001

Conclusions: Prevention and reduction of burn wound infection incidence begins with an understanding its risk factors. We have confirmed an association of early blood transfusion with this infectious complication, which indicates that limited use of blood transfusions early in the resuscitation may lead to a decrease in burn wound infections. We have also shown an association of burn wound infection with delayed transfer. Delayed transfer to definitive treatment may lead to increased burn wound infection because of the rapid bacterial colonization of the injured skin and delayed initiation of treatment indicating the importance of prompt transfer to definitive care.



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LAPAROSCOPIC GASTROPEXY FOR THE MANAGEMENT OF OBSTRUCTED GASTRIC VOLVULUS IN HIGH OPERATIVE RISK PATIENTS

Yates RB, Wright AS, Hinojosa MW, Oelschlager BK

Background: Obstructive gastric volvulus is frequently associated with paraesophageal hernia (PEH). Traditionally, obstructive gastric volvulus has been managed with reduction of the volvulus and repair of the PEH. This is an operation that takes significant time and can be associated with high morbidity and mortality. Consequently, high operative risk patients with acute or chronic gastric volvulus pose a particular challenge to surgeons. In these patients, we perform laparoscopic anterior abdominal wall gastropexy to relieve the gastric obstruction and prevent recurrence of volvulus. This case series reports our experience with this operation.

Methods: Between 2007 and 2013, we operated on 368 patients for symptomatic PEH. Of these, 11 patients presented with severe gastric obstruction (acute or chronic) and were considered too ill to tolerate formal PEH repair. In these patients, we performed a laparoscopic gastropexy with or without tube gastrostomy. From a prospectively collected database, we reviewed patient demographic information, medical comorbidities, and perioperative complications, including readmissions.

Results: Mean age was 78.1 years (range 50-92); 7 were men. All patients presented with acute or chronic gastric volvulus associated with primary PEH (nine patients) or recurrent PEH (two patients). Nine patients underwent laparoscopic gastropexy with tube gastrostomy. One patient underwent tube gastrostomy placement alone, and one patient underwent gastropexy alone. Median postoperative hospitalization was 2 days (range 1-39). Two patients required reoperation for prematurely displaced gastrostomy tubes. The first patient had undergone gastrostomy tube placement without sutured gastropexy. The tube became dislodged, it was replaced, and a gastropexy was performed. He was discharged to home on postoperative day 39 from his initial operation. The second patient was readmitted, underwent operative replacement of gastrostomy tube, and ultimately died from decompensated heart and pulmonary failure. Two additional patients were readmitted but required no intervention. One patient was lost to follow-up. Median clinical follow-up was 6 weeks (range 2-26). Excluding one death, all patients were asymptomatic at follow-up. One patient required nutrition via gastrostomy tube due to oropharyngeal dysphagia; 9 patients did not require supplemental nutrition and feeding tubes were removed between 6 and 12 weeks postoperatively.

Conclusions: We believe laparoscopic anterior abdominal wall gastropexy can successfully manage gastric volvulus in elderly and high-risk patients. Gastrostomy tubes were associated with significant morbidity and should be used selectively in patients likely to require postoperative nutrition supplementation.

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Das, Trina	
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LaGrone, Lacey	
Lipira, Angelo	

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Riggle, Kevin	
Simianu, Vlad	
Sood, Ravi	

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George Vance Foster Professor & Chair
Department of Surgery
University of Pittsburgh

2012

Gerald Fried, MD, FRCS(C), FACS
Professor of Surgery and Gastroenterology
Adair Family Chair of Surgical Education
Montreal General Hospital

2010

Jeffrey B. Matthews, MD
Dallas B. Pheister Professorship of Surgery
Chair, Department of Surgery
Dean for Clinical Affairs,
Biological Sciences Division
The University of Chicago

2008

Timothy J. Eberlein, MD
Bixby Professor and Chair
Department of Surgery
Washington University School of Medicine

2006

Richard H. Bell, Jr., MD
Professor and Chair of Surgery
Feinberg School of Medicine
Northwestern University

2004

Michael T. Longaker, MD
Director of Children's Surgical Research in the
Department of Surgery
Stanford University School of Medicine

2002

Ori D. Rotstein, MD
Peter A. Crossgrove Chair in General Surgery
The University of Toronto

2000

Lazar J. Greenfield, MD
Frederick A. Collier Professor and Chairman
Department of Surgery
The University of Michigan

1998

Haile T. Debas, MD
Chancellor and Dean, School of Medicine
University of California at San Francisco

1996

Richard L. Simmons, MD
Vance Foster Professor and Chair
Department of Surgery
University of Pittsburgh

2013

Anthony Atala, MD
Director of the Wake Forest Institute for
Regenerative Medicine
The W.H. Boyce Professor & Chair of the Department of
Urology at Wake Forest University

2011

Julie A. Freischlag, MD
The William Stewart Halsted Professor
Chair, Department of Surgery
Surgeon-in-Chief, The Johns Hopkins Hospital
Baltimore, MD

2009

Michael W. Mullholland, MD, PhD
Frederick A. Collier Distinguished
Professor of Surgery
Chair, Department of Surgery,
University of Michigan School of Medicine

2007

Shukri F. Khuri, MD, MS (Hon.)
Professor of Surgery, Harvard Medical School
Chief, Cardiothoracic Surgery,
VA Boston Healthcare System
Vice Chairman, Department of Surgery, Brigham and
Women's Hospital

2005

Barbara L. Bass, MD
Professor of Surgery
Maryland University School of Medicine

2003

Michael G. Sarr, MD
Professor of Surgery
Mayo Clinic Rochester

2001

John Mannick, MD
Moseley Distinguished Professor of Surgery
Harvard Medical School, Brigham & Women's Hospital

1999

Samuel A. Wells Jr., MD, FACS
Executive Director
American College of Surgeons

1997

Murray F. Brennan, MD
Alfred P. Sloan Chair in Surgery
Memorial Sloan-Kettering Cancer Center

1995

Judah Folkman, MD
Julia Dyckman Andrus Professor of Pediatric Surgery
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