

A background image of a laboratory scene. A person with long dark hair, wearing a white lab coat and blue gloves, is working at a lab bench. They are using a pipette to transfer liquid into a multi-well plate. In the foreground, a microscope is visible with a petri dish on its stage. Various lab equipment, including a centrifuge and storage containers, are scattered on the bench. The overall tone is professional and scientific.

UW Medicine

DEPARTMENT
OF SURGERY

**2019 RESEARCH DAY &
25TH ANNUAL
HELEN & JOHN
SCHILLING LECTURE**

AGENDA

6:45–7:15am	Breakfast & Registration	
7:30am	Welcome: Douglas E. Wood, MD, FACS, FRCSEd Introduction: David R. Flum, MD, MPH	
7:40am	Dara Horn, MD: Improving Protein Supplementation In The Critically Ill	Page 8
7:55am	Y. David Seo, MD: Blockade Of Cxcr4 Enhances Anti-Pd-1 Dependent Cd8 ⁺ T Cell Immunity Against Human Pancreatic Adenocarcinoma By Overcoming Intratumoral Immune Exclusion	Page 9
8:10am	Amir Ghaffarian, MD: Prognostic Implications Of Diagnosing Frailty And Sarcopenia In Vascular Surgery Practice: Function Versus Form	Page 10
8:25am	Lisa Hysa, BS: The Utilization Of Extended Criteria Donors In Liver Transplantation Does Not Affect Patient And Graft Survival	Page 11
8:40am	John Monu, MD: Changes In The Management Of Small Bowel Obstruction And Long-Term, Recurrence-Related Healthcare Utilization	Page 12
8:55am	Proceed to Poster Session 1	
9:00am	Elissa Butler, MD: Association Of Blood Component Ratios With 24–Hour Mortality In Injured Children Receiving Massive Transfusion	Page 13
9:05am	Erin Fennern, MD, MPH: Post–Discharge Chemoprophylaxis And Venous Thromboembolism Following Bariatric Surgery	Page 14
9:10am	Jason Hurd, MD: A Reliable Method For Renal Volume Measurement And Its Application In Fevar	Page 15
9:15am	Faculty presentation: Grant O’Keefe, MD, MPH Research Training in Basic Science Research	Page 7
9:30am	Kate Stadel, MD: The Challenge Of Diagnosing Perforated Appendicitis With Computed Tomography	Page 16
9:45am	Kavita Pandit, MD: The Hyperglycemia Paradox Of Surgical Complications	Page 17
10:00am	Jake Hemmingway, MD: Lowering The Ankle Brachial Index Threshold In Blunt Lower Extremity Trauma May Prevent Unnecessary Imaging	Page 18
10:15am	Shane Morrison, MD, MS: Prospective Quality Of Life Outcomes After Facial Gender–Affirming Surgery: An International Multi–Center Study	Page 19
10:30am	Proceed to Poster Session 2	
10:35am	Jennifer Minneman, MD: High Prevalence Of Asymptomatic Esophageal Motility Disorders And GERD In A Bariatric Surgery Population	Page 20
10:40am	Arezou Abassi, MD: A Phase 2 Trial Of Lanreotide For The Prevention Of Postoperative Pancreatic Fistula	Page 21
10:45am	Christopher Crowe, MD: Global Burden Of Hand Trauma: Trends Of Fracture And Digit Amputation, 1990–2017	Page 22
10:50am	Jenny Yu, MD: Mastectomy With Immediate Breast Tissue Expander Reconstruction: The University Of Washington Experience	Page 23



10:55am	Daniel Cho, MD, PhD: Patient Representation in Plastic Surgery Literature: Are We Appropriately Depicting Diversity?	Page 24
11:10am	Elissa Butler, MD, Is Presenting As Co-Author In Absence Of First Author, Greg Lisse, MD: Changing The Systolic Blood Pressure Threshold For Trauma Team Activation In Older Adults	Page 25
11:25am	Anna Ohlsson, MD: Radiation Safety In Vascular Surgery Training And Practice: A Survey of Experience and Exposure	Page 26
11:40am	Rebecca Ur, MD: Prevalence Of Chronic Opioid Use In Patients With Peripheral Arterial Disease Undergoing Lower Extremity Interventions	Page 27
11:55am	Sara Daniel, MD: Evaluating The Role Of Hypoxia In Anti-Tumor Immune Responses To Adenocarcinoma	Page 28
12:15–1:00pm	Break for Lunch	
1:05pm	Proceed to Poster Session 3	
1:10pm	Ben Massenburg, MD: Understanding Changes in the Global Burden of Orofacial Clefts from 1990 to 2017	Page 29
1:15pm	Barclay Stewart, MD, MscPH: A Legislative Framework To Address Chemical Assault	Page 30
1:20pm	Mark Thomas, MD: A Low-Cost Simulation Model And Instructional Video For Escharotomy Training	Page 31
1:25pm	Matthew Bartek, MD, MPH: Improving Operating Room Efficiency: A Machine Learning Approach To Predict Case-Time Duration	Page 32
1:30pm	Faculty presentation: Farhood Farjah, MD, MPH Research Training Clinical Research	Page 7
1:45pm	Brian Cook, MD: Crossmatches, Donor-Specific Antibodies And Antibody-Mediated Rejection In Liver Transplant Recipients	Page 33
2:00pm	Kevin Labadie, MD: Adoptive Transfer Of Genetically Engineered Macrophages To Reinvigorate Endogenous T Cell Responses Against Advanced Gastrointestinal Cancer	Page 34
2:15pm	Kevin Sullivan, MD: IL-10 Blockade Reactivates Anti-Tumor Immunity In Human Colorectal Cancer Liver Metastases	Page 35
2:30pm	Closing: David R. Flum, MD, MPH	
2:50–3:25pm	Intermission Break	
3:30–4:30pm	25th Annual Schilling Lecture – Mary Hawn, MD, MPH The Science Of Big Data And Promises Of Personalized Medicine	

INTRODUCTION



**Douglas E. Wood, MD,
FACS, FRCSEd**
*The Henry N. Harkins
Professor and Chair*

Welcome to the 25th Annual Department of Surgery Research Symposium and Schilling Lecture. This is an opportune moment to reflect on both the phenomenal quality of research in the department and the distinguished group of scholars who have joined us as lecturers and visiting faculty over the years. The Schilling lecturers represent the best and brightest across the spectrum of clinical and research disciplines in surgery. Their lectures inspire our residents and faculty and their engaged participation in the resident research symposium celebrates the work of our trainees. The resident research symposium and the lectureship are made possible by a generous gift from the late Helen Schilling in honor of her husband Dr. John Schilling. The Schillings were deeply committed to teaching, scholarship and research and this event where residents showcase their research supported by faculty mentors—is a great aspect of their legacy. It is with tremendous pride and gratitude that we carry on this tradition and look forward to doing so for years to come.



David R. Flum, MD, MPH
*Associate Chair for
Research, Professor of
Surgery, Associate Chief
Medical Officer,
UW Medicine*

This year we host as our Schilling lecturer Mary Hawn, MD, MPH, Professor of Surgery and Chair of the Department of Surgery at Stanford University. In today's Lecture, "The Science of Big Data and Promises of Personalized Medicine." Dr. Hawn will discuss the current state of big data in healthcare and potential uses for the future.

The Schilling Research Symposium is a forum for bringing together faculty, residents, fellows, students, and friends to share the innovative research happening 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. We view this day as a celebration of the passion for research that exists within our Department. Each and every member of the Department plays a critical role in the success of our research mission and we are grateful for the hard work and dedication of our staff, faculty, and trainees who make events like this possible. This year's symposium format will again feature both podium and poster presentations, as well as assigned discussants for the plenary session. Tonight, we will honor Dr. Hawn and all participants and their faculty mentors, and present prizes to the top poster and oral presenters.

We are pleased that you are joining us and hope that you find today's events both informative and inspiring.

Sincerely,

A handwritten signature in black ink, appearing to read "Doug Wood".

Douglas E. Wood, MD, FACS, FRCSEd
The Henry N. Harkins Professor and Chair
Department of Surgery
University of Washington

A handwritten signature in black ink, appearing to read "David Flum".

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

MARY HAWN, MD, MPH

Mary Hawn, MD, MPH, is a Stanford Medicine Professor of Surgery and Chair of the Department of Surgery at Stanford University. Dr. Hawn, a native of Michigan, received her education and general surgery training at the University of Michigan. Following residency, she pursued a fellowship in minimally invasive surgery at Oregon Health and Science University. Her clinical area of specialty is minimally invasive foregut surgery. She is a funded health services researcher and her projects focus on quality measurement and policy in surgical populations. She is a Director for the American Board of Surgery and serves on the editorial board of *Annals of Surgery* and the *Journal of the American College of Surgeons*. Dr. Hawn has several additional leadership roles in American Surgery including Treasurer for the Surgical Society of the Alimentary Tract, Treasurer for the James the IV Society and District Representative for the Western Surgical Association. She is also the co-Editor of a new surgical textbook *Operative Techniques in Surgery*.



Mary Hawn, MD, MPH
Professor of Surgery and Chair
of the Department of Surgery
at Stanford University

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 named 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 went on to become chairs. 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 chair, 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 professional association through the years in Oklahoma and Washington. They were married in 1979. Mrs. Schilling 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.

Special Guest Judge



Mary Hawn, MD, MPH
Professor of Surgery and Chair
of the Department of Surgery
at Stanford University

Department of Surgery Research Leadership



**Douglas E. Wood, MD, FACS,
FRCSEd (ad hom)**
The Henry N. Harkins Professor and Chair

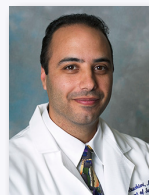


David R. Flum, MD, MPH
Associate Chair for Research,
Professor of Surgery

Research Leadership Committee



Saman Arbabi, MD, MPH
Professor



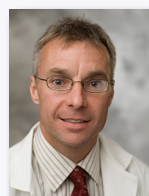
Joseph Cuschieri, MD
Professor



Nicole Gibran, MD
Professor



Ronald Maier, MD
Professor, Division Chief



Grant O'Keefe, MD, MPH
Professor



Robert Sawin, MD
Professor, Division Chief



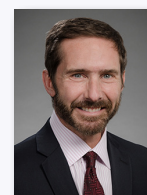
Eileen Bulger, MD
Professor



Farhood Farjah, MD, MPH
Associate Professor



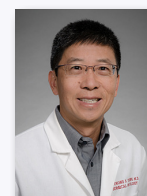
Danielle Lavalley, PharmD, PhD
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Michael Mulligan, MD
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Kimberly Riehle, MD
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Raymond Yeung, MD
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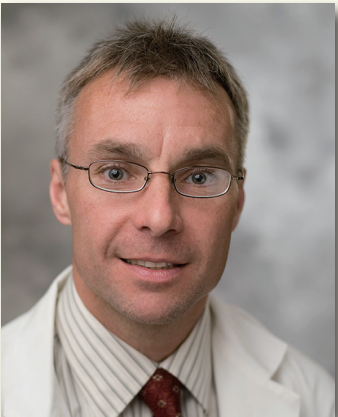
FEATURED DEPARTMENT OF SURGERY FACULTY



Farhood Farjah, MD, MPH

Associate Professor, Division of Cardiothoracic Surgery

Dr. Farjah's research focuses on quality improvement, comparative-effectiveness, and value optimization. His examination of outcomes and processes and structures of care for lung cancer patients has led to refinements to national quality measures for thoracic surgery, influenced practice guidelines recommending specialty surgical care, and informed the development of regional and national quality improvement initiatives in thoracic oncology. Dr. Farjah's work in comparative-effectiveness spans a wide variety of topics and conditions including evaluation of incidentally detected lung nodules, surgical approaches to pulmonary resection, surgical versus endoscopic management of achalasia, alvimopan use after colorectal surgery, and post-discharge chemoprophylaxis for venothromboembolism in bariatric patients. His work in value optimization develops and validates the use of risk-prediction models and biomarkers to guide more selective use of diagnostic tests in the care of lung cancer patients. Dr. Farjah's research has been funded by the National Cancer Institute, CHEST Foundation, and Fred Hutch/UW Cancer Consortium.



Grant O'Keefe, MD, MPH

Professor, Division of Trauma, Burn & Critical Care Surgery

Dr. O'Keefe is a Professor of Surgery and Adjunct Professor of Neurological Surgery, Orthopedics and Sports Medicine and is based at Harborview Medical Center. He received his MD in 1988 at the University of Alberta. His MPH was obtained from the University of Washington in 1994. He is a fellow of the American College of Surgeons and board certified in surgery and surgical critical care. Dr. O'Keefe's research spans three general areas and aims to understand the biology of critical illness and apply new knowledge to patient care. First, his research program has aimed to study the role of genetic variation in determining human inflammatory responses to infection. This work has been supported by the National Institutes of Health and the Department of Defense. Second, he has led and collaborated on studies aimed at understanding how the body responds to more severe infection and injury. These studies indicate that a systemic suppression of inflammation is an advantageous response, but one that, if excessive, may lead to compromise of immune functions needed to limit bacterial invasion. Dr. O'Keefe's third area of investigation builds upon a clinical interest in artificial nutritional support. He applies system-wide approaches to understanding the metabolic response to injury and towards the future of personalized nutritional support in critically ill patients.

IMPROVING PROTEIN SUPPLEMENTATION IN THE CRITICALLY ILL

Horn D, Shelton M, O'Keefe G

Background: Critical illness is often characterized by a period of starvation, hypercatabolism, and marked proteolysis. Protein supplementation has been associated with lower rates of infection and improved mortality in ICU patients, but the appropriate timing and composition remains debated. Currently, a weight-based recommendation of 2gm protein/kg/day is used to predict protein requirements and guide therapy, but this is based on expert opinion and has not been evaluated in a randomized control trial. Protein catabolic rate (PCR) is a measure of protein breakdown and can be estimated using total urinary nitrogen excretion (TUN). TUN is also used to quantify how well protein delivery meets demand. This study aims to determine whether protein supplementation improves nitrogen balance, and whether weight accurately predicts protein requirements in critically ill patients.

Methods: 276 adult trauma and surgical intensive care unit patients were randomized to receive either 2gm/kg/day of enteral protein independent of caloric intake, or standard nutritional support. This analysis examined 96 randomized patients who underwent a 24-hour urine collection for calculation of TUN during the first two weeks of hospitalization. PCR is directly proportion to TUN ($\text{PCR} = \text{TUN} * 6.25 + 2$). Nitrogen balance (NB) is the difference between nitrogen intake from enteral protein, and nitrogen excretion in the form of TUN ($\text{NB} = \text{Protein intake} / 6.25 - \text{TUN} + 2$). Simple and multiple linear regression were performed to identify clinical factors associated with PCR. Protein intake, and nitrogen balance were compared between treatment groups using the Mann-Whitney *U* test.

Results: The treatment group received significantly more enteral protein ($p < 1e-08$). Greater protein supplementation was associated with an improved nitrogen balance compared to controls (Figure 1), and patients in the treatment group were more likely to achieve a neutral or positive nitrogen balance ($\text{RR} = 1.77$, $p = 0.018$). Weight accounts for only a small proportion of the variability in protein catabolic rate (Figure 2). On multiple regression analysis, age, sex, weight, protein intake, and ICU day of TUN measurement were all significantly associated with PCR ($p < 0.05$), and together explained roughly half of the variation in PCR ($R^2 = 0.47$).

Conclusions: Aggressive protein supplementation is feasible and is associated with improved nitrogen balance in critically ill patients. However, weight-based guidelines for predicting protein requirements appear unreliable as weight alone accounts for little of the variability in PCR, and additional clinical characteristics only modestly improve predictions of PCR. Alternative methods to better quantify and trend protein catabolism over time are needed to further personalize nutrition delivery.



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Faculty Mentor

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Hometown

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Medical School

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Research Interests

Trauma, critical care, translational medicine

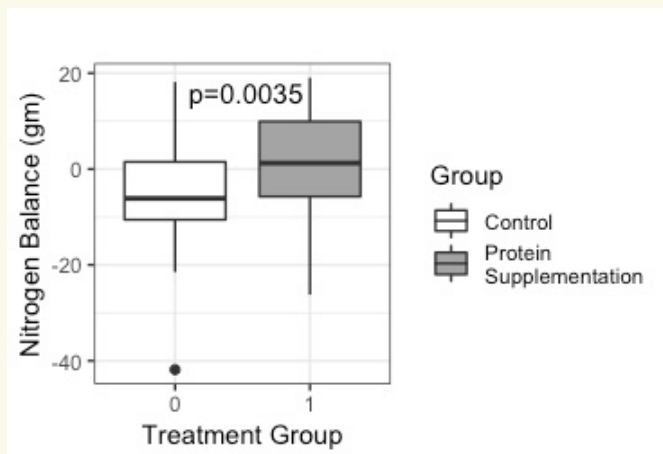


FIGURE 1

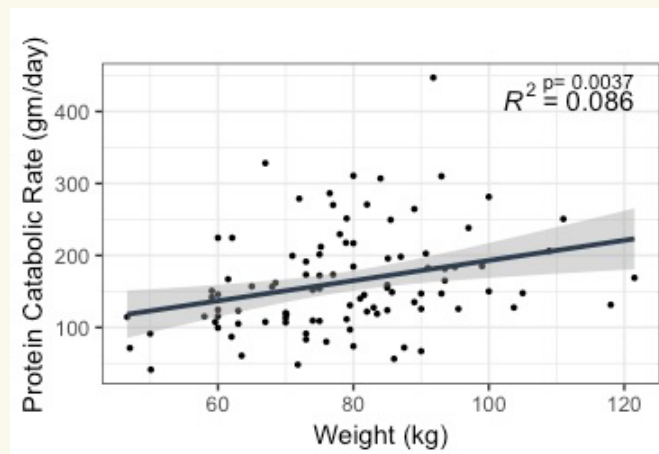
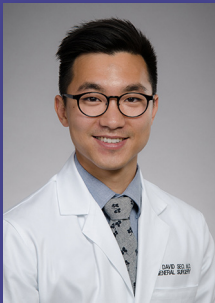


FIGURE 2



Y. David Seo, MD

General Surgery, R3

Faculty Mentor

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Research Interests

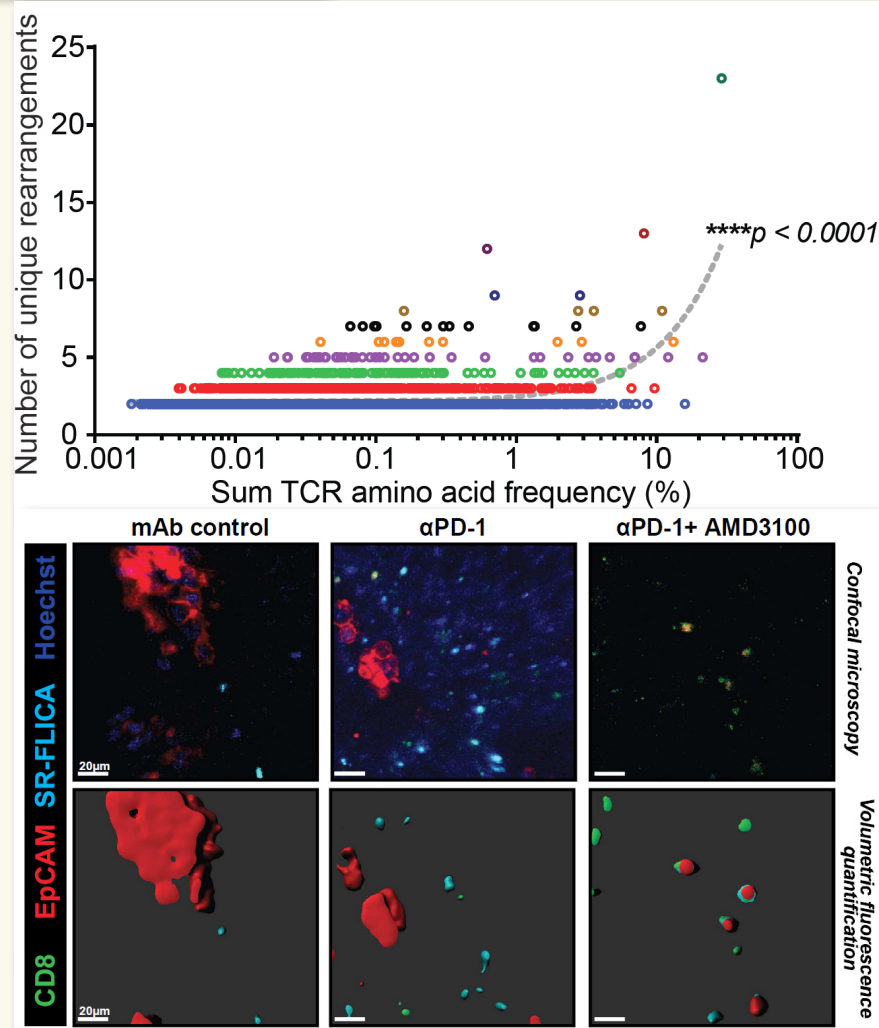
Immuno-oncology, T cell adoptive therapy

BLOCKADE OF CXCR4 ENHANCES ANTI-PD-1 DEPENDENT CD8+ T CELL IMMUNITY AGAINST HUMAN PANCREATIC ADENOCARCINOMA BY OVERCOMING INTRATUMORAL IMMUNE EXCLUSION

Seo YD, Jiang X, Sullivan KM, Jalikis F, Smythe KS, Abbasi A, Vignali M, Park JO, Daniel SK, Pollack SM, Kim TS, Yeung RSW, Crispe IN, Pierce RH, Robins H, Pillarisetty VG

Background: Human pancreatic ductal adenocarcinoma (PDA) remains a disease of high morbidity and mortality despite recent advances in immunotherapeutics. Tumors demonstrate an element of immune exclusion, as effector cells are often found outside the immediately juxtatumoral compartments. Here, we demonstrate the first direct evidence of tumor-reactive T cells in the PDA microenvironment.

Methods: FFPE blocks of human PDA samples were taken from patients after resection and examined using a combination of multiplex immunohistochemistry (mIHC) and T cell receptor (TCR) β chain sequencing. mIHC images were annotated by an expert pathologist to delineate juxtatumoral compartments. TCR sequencing was analyzed using the Adaptive Biotechnologies immunoSeq platform to determine relative frequencies of DNA and amino acid sequences among all T cells. To test the effect of combination immunotherapy on PDA, tumor slice cultures using 250um slices of fresh resected PDA tumors were grown and treated in culture. Subsequent slices were imaged using combination of live immunofluorescence microscopy and standard IHC.



Results: We demonstrated that the juxtatumoral compartment of PDA shows less infiltration of CD8⁺ T cells. TCR sequencing revealed evidence of clonal expansion; in addition, high frequency TCR amino acid sequences were coded by multiple disparate DNA sequences, suggesting convergent evolution toward the same target. In the *ex vivo* organotypic tumor slice culture model, CXCR4 blockade abrogates sequestration of CD8⁺ T cells in the stromal compartment, while combination with PD-1 blockade leads to both trafficking of CD8⁺ T cells to tumor cells and resultant tumor cell apoptosis. These findings were consistent across a large number of individual tumors, suggesting that this mechanism may be relevant to the majority of patients.

Conclusions: Taken together, these results show that tumor-reactive CD8⁺ T cells within the human PDA microenvironment are highly abundant and can be activated against carcinoma cells through the rational combination of clinically-available drugs.

PROGNOSTIC IMPLICATIONS OF DIAGNOSING FRAILITY AND SARCOPENIA IN VASCULAR SURGERY PRACTICE: FUNCTION VERSUS FORM

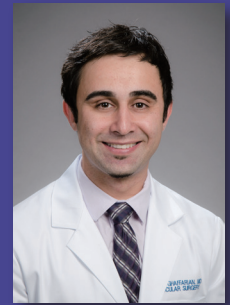
Ghaffarian AA, Foss WT, Kraiss LW, Smith BK, Griffin CL, Sarfati MR, Brooke BS

Background: Frailty and sarcopenia are related but independent conditions commonly diagnosed in older patients that can be used to assess their ability to tolerate the stress of major vascular surgery. In order to be used for surgical decision making, however, it is important to know the prognostic implications associated with these conditions. The study was designed to assess the association between frailty and sarcopenia phenotypes with long-term survival among patients undergoing surgical and non-surgical management of vascular disease.

Methods: We retrospectively reviewed all patients who presented to the vascular surgery clinic at an academic hospital between December 2015 and August 2017 who underwent prospective frailty assessment with the Clinical Frailty Scale and who had undergone abdominal CT scan within the prior 12-months. A single axial CT-image at the caudal end of the 3rd-lumbar vertebrae was assessed to measure cross-sectional areas (cm²) of skeletal muscle. Sarcopenia was defined using established criteria for male and female patients. After stratifying patients by frailty and sarcopenia diagnoses, along with comorbidities, the association with all-cause mortality was analyzed using Kaplan Meier curves and Cox regression models.

Results: A total of 415 patients underwent both frailty and sarcopenia assessment, of which 112 (27%) met sarcopenia criteria alone, 48 (12%) met only frailty criteria, and 56 (13%) met criteria for both phenotypes. There were 199 (48%) controls who met neither criteria. Vascular Surgery was performed in 167 (40%) patients following frailty & sarcopenia assessment, whereas 248 (60%) patients were managed non-operatively with median (IQR) follow-up after CT imaging of 1.5 (1.1-2.2) years. Patients diagnosed with either phenotype were older (mean 65-yrs vs. 59-yrs; $P<0.001$), and more likely to be male (69% vs. 54%; $P<0.001$) when compared to patients without sarcopenia or frailty. Long-term survival was significantly decreased for patients diagnosed with either frailty alone or frailty and sarcopenia who underwent surgical (Figure A) or non-surgical management (Figure B). In multivariate regression models, however, frailty was the only independent variable (HR: 7.7, 95%CI: 3.2-18.7; $P<0.001$) that predicted mortality.

Conclusions: Frailty and sarcopenia can both be used to predict long-term survival among patients presenting for vascular surgery management. However, our data indicates that frailty alone is the only independent predictor associated with mortality and has the strongest prognostic implications.



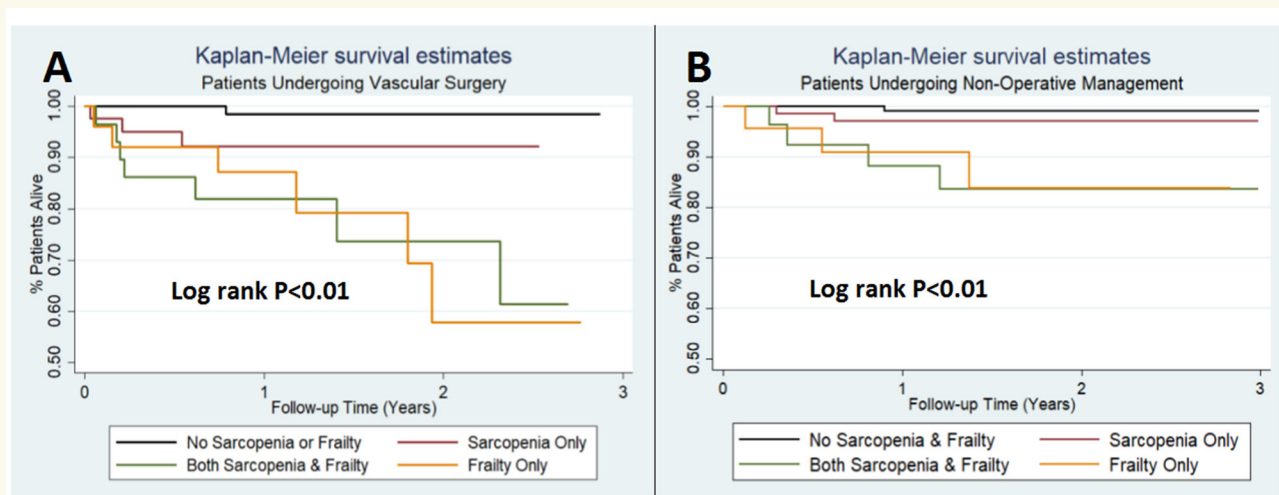
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Research Interests
Clinical Outcomes Research





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Research Interests
Expanding Liver
Transplant Donor Pool

THE UTILIZATION OF EXTENDED CRITERIA DONORS IN LIVER TRANSPLANTATION DOES NOT AFFECT PATIENT AND GRAFT SURVIVAL

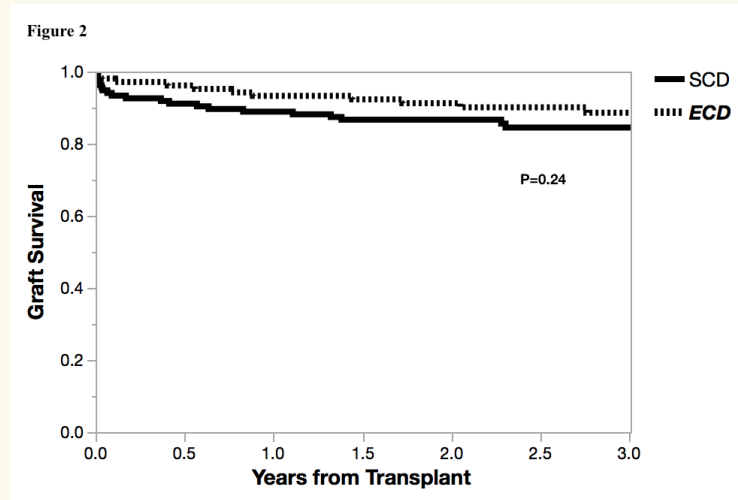
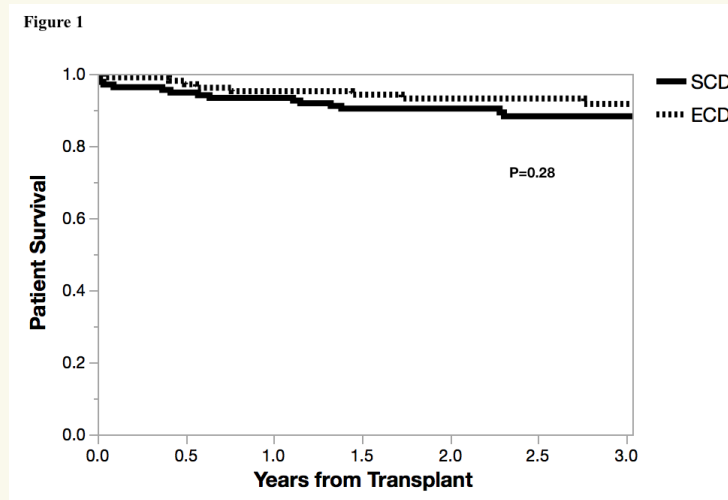
Hysa L, Perkins J, Montenovo M

Background: Increasing organ scarcity has motivated transplant centers to relax restrictions to donation creating the term “extended-criteria donor” (ECD). Definitions of these terms are not widely accepted. Restrictions focus on potential recipient risk categorized as impaired allograft function and/or donor-transmitted disease. Due to a better understanding in the utilization of these grafts, we hypothesize that both patient and graft survival associated with utilization of liver grafts from ECD will be similar to standard criteria donors (SCD).

Methods: Retrospective cohort analysis of adult liver transplant recipients performed at UWMC between January 1, 2014 and December 31, 2016. Clinical data was obtained from transplant database at UW. Analysis was limited to transplant recipients age 18 years and older who received primary liver transplant. Patients with re-transplantation, multi-organ transplants and living donor liver recipients were excluded.

Results: We identified 104 ECD and 135 SCD recipients. Mean age for ECD donor is 37.6 ± 14.2 years old and SCD donor is 32.5 ± 13.5 years old ($p=0.002$). ECD livers have shorter mean cold ischemia time (7.1 ± 2.0 hours vs. 8.0 ± 2.5 ; $p=0.003$). Outcomes show that rate of organ dysfunction, re-transplantation, length of hospital stay and liver enzymes are not different between groups. Kaplan Meier patient and graft survival show no difference between recipient groups (figure 1 & 2). Cox proportional hazards model show ECD use does not lead to worse graft or patient survival.

Conclusions: There is no difference between ECD and SCD in both patient and graft survival. The liver transplant community should reconsider utilization of these grafts in an era of scarce organ availability and high wait list mortality.



CHANGES IN THE MANAGEMENT OF SMALL BOWEL OBSTRUCTION AND LONG-TERM, RECURRENCE-RELATED HEALTHCARE UTILIZATION

Monu JI, Symons RG, Davidson GH, Flum DR

Background: Small bowel obstruction (SBO) is increasingly managed expectantly, operating only on those with bowel compromise, but the effectiveness of this approach compared to the historical standard of early operation has yet to be evaluated. Different approaches to SBO management may impact the rate of recurrence and healthcare utilization (HCU). We compared long-term, SBO recurrence-related HCU following operative and non-operative management of index SBO.

Methods: A retrospective cohort study (Washington State Comprehensive Hospital Abstracting Record System data, 1987-2015) with index SBO identified using ICD-9/10 codes (excluding non-adhesion causes) and surgical management defined using procedure codes. SBO-related recurrent hospitalization, hospital days, and inflation-adjusted charges were compared between those with/without operation at index SBO using time-to-event analysis.

Results: Of 60,933 patients with index SBO (age 65 ± 17 , 57% female, follow-up 3 years [IQR, 0.7-8]), operation was performed in 23% (27% in 1987, 16% in 2015, $p < 0.01$). Patients undergoing operation had lower likelihood of recurrence (16% vs 20%, $p < 0.01$), fewer recurrences (0.28 vs 0.39, $p < 0.01$), longer time to first recurrence (672 versus 343 days, $p < 0.01$), and were less likely to have ≥ 3 recurrences (2.3% vs 3.8%, $p < 0.01$). There were no differences in recurrence requiring operation ($p = 0.66$), median hospital days ($p = 0.11$) and charges ($p = 0.30$).

Conclusions: Although operative management of index SBO was associated with fewer SBO recurrences, subsequent recurrences did not require operation more often and HCU and costs were similar to those not having operation. Recurrence-related HCU may be an important consideration in comparative effectiveness evaluations of expectant vs early, operative management.



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Research Interests

Comparative Effectiveness,
Lung Cancer Screening,
Behavioral Economics



Elissa Butler, MD

HIPRC Research Fellow

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Research Interests

Geriatric Trauma, Trauma
Systems Management, Triage

ASSOCIATION OF BLOOD COMPONENT RATIOS WITH 24-HOUR MORTALITY IN INJURED CHILDREN RECEIVING MASSIVE TRANSFUSION

Butler EK, Mills BM, Arbabi S, Bulger EM, Vavilala MS,
Groner JJ, Stansbury LG, Hess JR, Rivara FP

Background: The optimum ratio of blood components for massive transfusion in pediatric trauma patients remains unknown. Our objective was to determine if higher plasma:RBC (red blood cell) and platelet:RBC ratios are associated with lower 24-hour mortality.

Methods: This was a retrospective cohort study using the Pediatric Trauma Quality Improvement Program Database from January 1, 2014, to December 31, 2016. Injured children (≤ 14 years) who received massive transfusion (≥ 40 mL/kg total blood products in initial 24 hours of treatment) were included ($n=583$). Using multivariable Poisson regression analysis, the association between ratios of plasma:RBC and platelet:RBC and 24-hour mortality were assessed.

Results: Overall 24-hour mortality was 19.7% among pediatric patients receiving massive transfusion (95% CI: 16.6 to 23.2%). There was 51% (aRR 0.49, 95% CI: 0.27 to 0.87, $p=0.02$) lower risk of death at 24 hours for the high ($\geq 1:1$) plasma:RBC group and a 40% (aRR 0.60, 95% CI: 0.39 to 0.92, $p=0.02$) lower death risk for the medium ($\geq 1:2$ and $<1:1$) plasma:RBC group compared to the low ratio group ($<1:2$). High platelet:RBC ratio was not associated with decreased mortality (aRR: 0.94, 95% CI 0.51 to 1.71, $p=0.83$).

Conclusions: Massive transfusion with plasma:red blood cell ratio $\geq 1:2$ was associated with improved 24-hour survival in severely injured pediatric trauma patients. While these findings represent the largest study evaluating blood product ratios in pediatric trauma patients, further studies are needed to determine if higher plasma:red blood cell ratios improve overall outcomes.

POST-DISCHARGE CHEMOPROPHYLAXIS AND VENOUS THROMBOEMBOLISM FOLLOWING BARIATRIC SURGERY

Fennern EB, Chen J, Khandelwal S, Verdial F, Cook T, Wolff EM, Farjah F

Background: One in ten surgical patients who experience a post-operative venous thromboembolic event (VTE) dies. Bariatric surgery patients often have multiple VTE risk factors, such as complex abdominal surgery, morbid obesity, and associated co-morbid conditions. Prior studies show that roughly 80% of VTEs in bariatric surgery patients occur after discharge, logically leading to the idea that post-discharge prophylaxis may reduce the risk of these events. Given their rarity, it is difficult to study the relationship between incident VTEs and post-discharge chemoprophylaxis. Currently, there is no high-level evidence to support decision-making among bariatric patients regarding whether or not to prescribe post-discharge chemoprophylaxis. Moreover, little is known about current practice patterns in the community. We hypothesized that a minority of bariatric surgery patients receive post-discharge VTE chemoprophylaxis, and that post-discharge chemoprophylaxis is associated with a lower risk of post-discharge VTE.

Methods: We performed a retrospective cohort study (2007–2015) of adult patients, 18 to 64 years of age, who underwent either a laparoscopic sleeve gastrectomy or a gastric bypass (either open or laparoscopic) using commercial insurance claims data from the Truven Health MarketScan database. We excluded patients with outpatient pharmacy claims for anti-coagulation medication in the 90 days prior to surgery, or with an International Classification of Diseases, 9th Edition (ICD-9) diagnostic code for VTE during their index admission. We determined receipt of post-discharge heparin (unfractionated or low molecular weight) chemoprophylaxis for up to 35 days after discharge, as derived from outpatient pharmacy claims data. We defined post-discharge VTEs as follows: either an ICD-9 diagnostic code for VTE, or both a Current Procedural Terminology code for VTE diagnostic imaging *and* a subsequent outpatient pharmacy claim for anti-coagulation medication.

Results: Among 43,493 patients (median age 45 years; 78% women; 77% laparoscopic gastric bypass; 17% laparoscopic sleeve gastrectomy; 6% open gastric bypass), only 2,587 (6%) received post-discharge chemoprophylaxis. A total of 224 (0.52%) patients suffered a post-discharge VTE event within 90 days of surgery, of whom 10 received post-discharge chemoprophylaxis. The 90-day post-discharge VTE rate was lower in patients who received post-discharge chemoprophylaxis compared to those that did not (0.35% vs. 0.52%), but the unadjusted difference was not statistically significant (p -value=0.35). This unadjusted difference corresponds to a non-significant relative risk reduction of 26% (OR 0.74, 95% confidence interval of 0.39 to 1.39).

Conclusions: In this bariatric surgery patient population of privately insured patients, post-discharge chemoprophylaxis was infrequently prescribed and not associated with a lower risk of VTE. Potential explanations for these findings include: 1) the absence of a true effect of chemoprophylaxis on risk reduction; 2) inadequate adjustment for confounding factors; and/or 3) insufficient sample size. With this dataset, our next step is to conduct a propensity score-adjusted analysis to control for confounding.



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A RELIABLE METHOD FOR RENAL VOLUME MEASUREMENT AND ITS APPLICATION IN FEVAR

Hurd J, Chen X, Tatum B, Katsman D, Singh N, Zierler RE, Caps M, Starnes B

Background: Renal volume has been shown to decline in the sixth decade of life and beyond. We sought: 1) to assess the inter-rater reliability for manually measuring renal volume using computed tomography and 2) to assess changes in renal volume over time as it relates to Fenestrated EVAR (FEVAR).

Methods: This study was conducted as part of a physician-sponsored IDE (#NCT01538056).

1) 30 consecutive kidneys of pre-operative FEVAR subjects were randomly measured by two independent raters using manual segmentation and TeraRecon (Foster City, CA) software (Figure 1). Renal volumes were calculated and compared. Cohen's Kappa was calculated for differences in renal volume of 1, 3, 5 and 10%.

2) Renal volumes were then recorded for 100 subjects undergoing FEVAR with follow up out to five years and then normalized by dividing the value by the subjects Body Surface Area (Du-Bois formula; $BSA = (W^{0.425} \times H^{0.725}) \times 0.007184$). Kidneys were divided into three groups and two sub-groups. Group A kidneys were those that were fed by a renal artery that had no fenestration and no stent. Group B were those kidneys fed by an artery with a fenestration but no stent and Group C were those kidneys fed by renal arteries that were stented through a fenestration. Finally, Group C was further sub-divided into those kidneys that had additional accessory renal arteries that were covered by the stent graft (Group C.1) and those kidneys without accessory renal arteries (Group C.2).

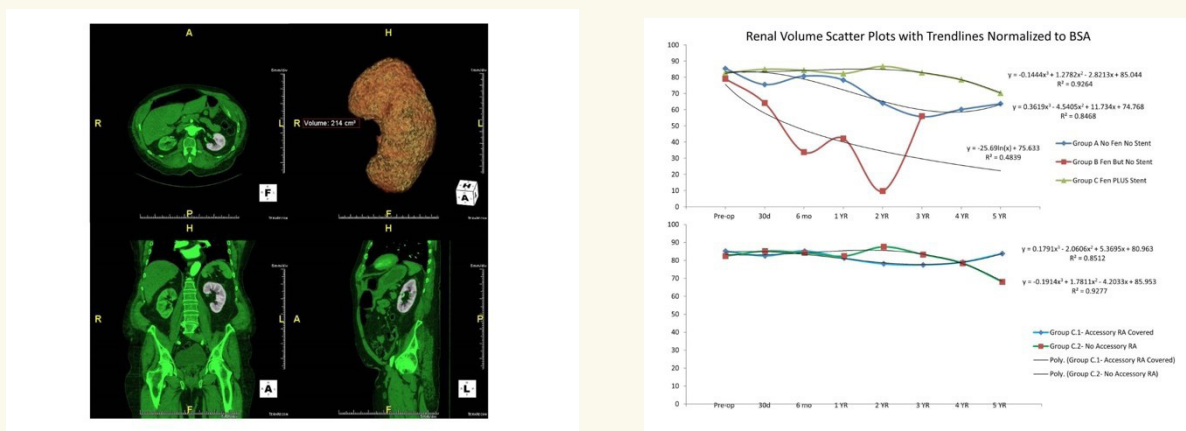
Results: 1) Inter-rater reliability (kappa) for manual renal volume measurement was 0.19, 0.63, 0.84 and 1.00 for renal volume differences of 1, 3, 5, and 10% respectively.

2) There were 10 kidneys in Group A, 7 kidneys in Group B and 172 kidneys in Group C. Group C.1 included 11 kidneys and Group C.2 included 161 kidneys. Scatterplots comparing Groups A, B and C AND C.1 and C.2 are shown in Figure 2.

Conclusions: Manual renal volume measurements are highly reliable and reproducible to within a 5% difference between raters. Renal volume decreases over time, regardless of whether the renal artery is stented or not. It appears that renal volume does not decline as rapidly when renal arteries are stented as part of FEVAR. Coverage of accessory renal arteries appears safe and does not significantly lead to decline in renal volume.

Figure 1. Manually segmented renal volume measurement using TeraRecon software

Figure 2. Renal volume scatter plots with trendlines normalized to BSA



THE CHALLENGE OF DIAGNOSING PERFORATED APPENDICITIS WITH COMPUTED TOMOGRAPHY

Stadeli KM, Pandit KP, Monsell SE, Talan DA,
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Background: Six European randomized controlled trials (RCTs) have demonstrated that treatment with antibiotics alone is safe for patients with uncomplicated appendicitis. Though localized perforation of the appendix is common, most studies excluded such patients, usually based on findings from computed tomography (CT). Given the common use of preoperative imaging for clinical treatment decision-making, we aimed to evaluate the accuracy of CT for perforation.

Methods: A 21-hospital network recruiting participants for the Comparison of Antibiotic Drugs and Appendectomy Trial assessed patients (without generalized peritonitis) undergoing operation within 24 hours of CT. Perforation was defined by diagnosis on either operative or pathology report. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of preoperative CT were calculated based on overall and specific findings of the report.

Results: Of 1024 participants (50% female, 62% white, mean age 38) with appendicitis, 18.3% (187/1024) had perforation diagnosed by operative or pathology report. Preoperative CT described 3.7% (38/1024) of cases as perforated (13% sensitive, 98% specific, PPV 63%, NPV 83%). Appendiceal diameter ≥ 12 mm and free fluid had the highest sensitivities (66%, 36% respectively), while cecal wall thickening, fat stranding, abscess, periappendiceal air, and hyperenhancement had sensitivities $<15\%$ (Table 1).

Conclusions: Using CT to select patients with appendicitis for antibiotic treatment will not exclude most with perforation. These findings demonstrate a limitation of preoperative CT to guide treatment decisions in appendicitis.

Table 1. Specific computed tomography findings in perforated and non-perforated appendicitis

Computed Tomography Finding N = 1024	^a Perforated N = 187	^a Nonperforated N = 837	^b P-value	Sensitivity	Specificity	PPV	NPV
Cecal wall thickening	18 (9.6%)	32 (3.8%)	0.002	9.7%	96.2%	36.0%	82.7%
Periappendiceal fat stranding (moderate or severe)	7 (3.7%)	4 (0.5%)	0.001 ^c	3.8%	99.5%	63.6%	82.3%
Abscess	8 (4%)	8 (1%)	0.003	4.3%	99.0%	50.0%	82.2%
Periappendiceal air	7 (4%)	4 (0.5%)	0.001 ^c	3.7%	99.5%	63.6%	82.2%
Simple free fluid	66 (35%)	233 (28%)	0.05	35.9%	72.1%	22.1%	83.3%
Hyperenhancement of appendix	25 (13%)	113 (14%)	$>.999$	13.5%	86.5%	18.1%	81.8%
Max appendiceal diameter							
<12 mm	54 (34%)	402 (60%)	$<.0001$	65.6%	60.5%	28.1%	88.1%
≥ 12 mm	103 (66%)	263 (40%)					
Missing	30 (16.0%)	172 (20.5%)					

^aCategorized by definition of perforation: diagnosis of perforation on either operative or pathology report.

^bP-value from Chi-square test unless noted otherwise.

^cp-value from Fisher's exact test.



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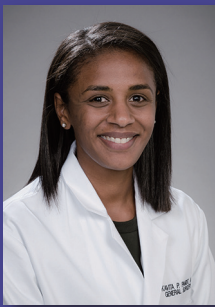
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Equitable Injury care, Physician-Patient Relationship, Patient-Centered Care



THE HYPERGLYCEMIA PARADOX OF SURGICAL COMPLICATIONS

Pandit KP, Thornblade LW, Cook T, Chen JY, Dellinger EP, Flum DR

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Improving Equity and
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Background: Although perioperative hyperglycemia is usually associated with diabetes mellitus (DM), two prior cohort studies have paradoxically found that, compared to patients with DM, non-DM (NDM) patients have greater risk of complications at similar levels of hyperglycemia. These studies were limited by selective blood glucose (BG) testing and use of insulin. We aimed to evaluate this “hyperglycemia paradox” in a cohort with nearly universal BG testing and routine insulin use.

Methods: A retrospective cohort study of a purposeful sample of surgical patients from 2013–2016. Perioperative BG and insulin data were obtained from clinical records. NSQIP (National Surgical Quality Improvement Project)–defined complications were obtained by trained abstracters.

Results: 91% of patients underwent BG testing (n= 4,466) and 66% had elevated BG (>140 mg/dL). Among DM patients (16%), 96% had hyperglycemia and 88% received insulin. Among NDM patients, 61% had hyperglycemia and 42% received insulin. Post-insulin BG was euglycemic (< 140 mg/dL) in 33% of patients who received insulin. Complications occurred in 16% and were more common in patients with DM (18% vs 15%, p= 0.02). At similar levels of hyperglycemia NDMs had higher rates of complications compared to DM patients (BG 140–179: 14% vs 10% p=.08, 180–250: 17% vs 24% p=.002, >250 40% vs 28% p=.007). In NDMs with hyperglycemia, complications were less common when receiving insulin at all levels of hyperglycemia except BG>250 (BG 140–179: 12% vs 15% p=.1, 180–250: 21% vs 30% p=.001), independent of post-insulin euglycemia (Table 1).

Conclusions: At similar levels of hyperglycemia NDM patients have worse outcomes than DM patients. Insulin, independent of euglycemia, reduces, but does not eliminate this risk. Potential reasons for this paradox are being evaluated including whether NDMs with hyperglycemia have greater inflammatory responses, underuse of insulin, or misclassification of undiagnosed DM.

Table 1. Postoperative Complications by Perioperative Blood Glucose Level

	Number Complications, n (%)		
	Blood Glucose (mg/dL)		
	140–179	180–250	>250
Complications, n (%) by Diabetic Status			
Diabetic (n=731)	11 (10%)	65 (17%)	56 (28%)
Nondiabetic (n=3,735)	178 (14%)	209 (24%)	67 (40%)
Complications Among Nondiabetics, n (%) by Insulin Treatment			
Not Treated with Insulin (n=27,59)	140 (15%)	99 (30%)	22 (35%)
Treated with Insulin (n=952)	38 (12%)	110 (21%)	45 (43%)
Euglycemic Following Insulin (n= 312)	19 (11%)	28 (22%)	6 (33%)
Hyperglycemic Following Insulin (n=640)	19 (13%)	82 (20%)	39 (45%)

LOWERING THE ANKLE BRACHIAL INDEX THRESHOLD IN BLUNT LOWER EXTREMITY TRAUMA MAY PREVENT UNNECESSARY IMAGING

Hemingway JF, Adjei EA, Desikan SK, Gross JA, Tran NT, Singh N, Starnes BW, Quiroga E



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Background: Current algorithms for the management of blunt lower extremity trauma recommend additional imaging if the ankle-brachial index (ABI) is less than 0.9. The aim of this study was to analyze lower extremity Computed Tomography Angiographies (CTAs) to determine the incidence and characteristics of patients sustaining vascular injury from blunt lower extremity trauma. We hypothesized that a lower ABI threshold can avoid unnecessary imaging without missing clinically significant vascular injury.

Methods: A single center, retrospective review of all consecutive patients who presented to a level 1 trauma center with blunt lower extremity trauma and underwent a CTA from January 2015–December 2017 was conducted. Baseline demographics, clinical features, and outcomes were recorded. Patients without documented ABIs were excluded. A receiver operator characteristic (ROC) curve was used to define the ABI threshold.

Results: 125 patients (133 injured limbs) met inclusion criteria. The mean age was 44 years (range 9–96), and 74% of patients were male. A vascular abnormality was identified on CTA in 65 limbs (49%), of which only 8 (12%) required intervention. The ABIs in these injured limbs were between 0 and 0.6 (Figure 1a). An ABI threshold of 0.6 maximized the balance between sensitivity (100%) and specificity (87%) and missed no injuries requiring revascularization (Figure 1b).

Conclusions: The ABI remains useful in evaluating blunt lower extremity trauma. A lower ABI threshold may avoid unnecessary imaging without missing vascular injuries. Further prospective studies are needed to validate the safety and effectiveness of a lower ABI threshold.

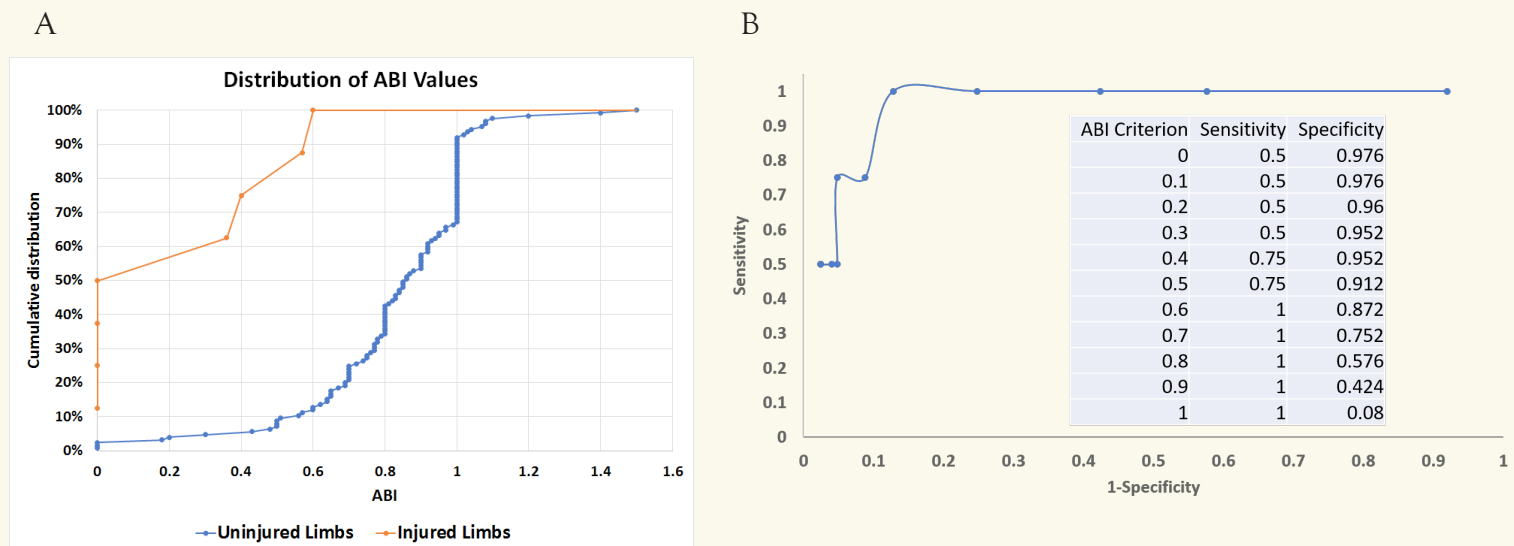


Figure 1: Cumulative distribution of ABI values among injured and uninjured limbs (1a), and the corresponding ROC curve with sensitivities and specificities for various ABI thresholds (1b).



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Gender-Affirming Surgery,
Patient-Reported Outcomes

PROSPECTIVE QUALITY OF LIFE OUTCOMES AFTER FACIAL GENDER-AFFIRMING SURGERY: AN INTERNATIONAL MULTI-CENTER STUDY

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Background: No data exist on the prospective outcomes of gender-affirming surgery, especially facial feminization surgery. This study set out to determine the effects of facial feminization surgery on quality of life outcomes for transgender or gender diverse patients.

Methods: In this prospective international multi-center cohort study, adult transgender or gender diverse patients suffering from dysphoria were enrolled from two separate centers in the United States or Europe. Facial feminization surgery outcomes quality of life score was calculated pre-operatively, one-week to one-month post-operatively, and greater than 6 months post-operatively. Photogrammetric measurements were taken at the same time points. Patient perceived pre-operative masculinity and femininity were recorded. Linear regression analyses were used for predictions of outcomes of quality of life after facial feminization surgery.

Results: Sixty-six adult transgender or gender diverse patients were enrolled in the study. Patients noted their brows, jaw, and chin were the most masculine aspects of their faces (54.5%, 33.3%, and 30.3%, respectively). The facial feminization surgery outcome quality of life score substantially increased between pre-operative and post-operative periods along with remaining stable at greater than 6 months post-operative (48.0 ± 12.3 pre-operatively versus $76.5 \pm 14.6 \geq 6$ months post-operatively, $p < 0.0001$). Patient satisfaction with facial feminization surgery remained stable in the post-operative period (one-week to one-month post-operative mean score, 3.1 ± 0.8 ; ≥ 6 month post-operative mean score, 3.0 ± 1.0 ; $p = 0.46$). Photogrammetric measurements were significantly more feminine after FFS. Only age was a significant predictor of facial feminization surgery outcome quality of life score ($\beta = -0.290$, $p = 0.006$).

Conclusions: Improved quality of life outcomes are seen after facial feminization surgery in this prospective study and correspond with similar changes in quality of life in previous retrospective studies. Quality of life and satisfaction remain stably improved in the long-term. Due to these findings, portions of facial gender-affirming surgery should be considered a medical necessity for patients with facial gender dysphoria and be covered by insurance.

HIGH PREVALENCE OF ASYMPTOMATIC ESOPHAGEAL MOTILITY DISORDERS AND GERD IN A BARIATRIC SURGERY POPULATION

Minneman JA, Chen JY, Ehlers AP, Nieblas–Bedolla E, Cruz MJ, Hale MR, Wright AS, Khandelwal S

Background: Gastroesophageal reflux disease (GERD) and esophageal dysmotility symptoms after laparoscopic sleeve gastrectomy (LSG) pose challenging clinical problems. Few centers assess for GERD or motility disorders prior to performing LSG. Prior studies demonstrate a high prevalence of esophageal motility abnormalities in morbidly obese patients (21–61%), but few of these studies were performed with high-resolution manometry (HRM) and most do not include patient symptomatology. We hypothesize that there is a high prevalence of undiagnosed motility disorders and GERD in a morbidly obese patient population being evaluated for sleeve gastrectomy.

Methods: We performed HRM and 24-hour pH testing in 122 consecutive patients considering sleeve gastrectomy in 2017. We retrospectively analyzed prospectively-collected data from the electronic medical record and symptom surveys filled out at the time of their studies. Motility disorders were defined based on the Chicago classification v3.0. GERD was defined by an abnormal DeMeester score (>14.7) on 24-hour pH manometry.

Results: Of all patients studied, 44/122 (36%) had a motility disorder. The most common condition was ineffective esophageal motility (65.9%). Other diagnoses included esophagogastric junction outflow obstruction (27.2%), jackhammer (hypercontractile) esophagus (4.5%) and diffuse esophageal spasm (2.3%). Patients with abnormal motility had a higher median BMI than those with normal motility (49 versus 45, $p=0.01$). Symptom survey data was available for 109/122 patients, including 82% of patients with motility disorders and 86% of patients with normal motility. Reported dysphagia was low regardless of whether the patient had a motility disorder (13.9%) or not (17.9%). Absence of dysmotility symptoms (dysphagia, chest pain, regurgitation) was similar for patients with motility disorders compared to those with normal motility (47.5% versus 50.7%, $p=0.87$). Abnormal DeMeester scores were seen in 38/122 (31.1%) patients, with 70% of these patients reporting heartburn. Additionally, heartburn was not limited to patients with abnormal DeMeester scores – 45% of patients with normal DeMeester scores also complained of heartburn ($p=0.04$).

Conclusions: There is a high prevalence of both motility disorders and GERD in patients being considered for LSG. Dysphagia and heartburn are unreliable in identifying abnormal esophageal motility and GERD in morbidly obese patients. When deciding whether to offer patients LSG, accurately diagnosing abnormal motility and pathologic GERD using HRM and pH testing may lead to improved preoperative counseling and patient selection.



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Pancreatic Cancer and
Liver Cancer

A PHASE 2 TRIAL OF LANREOTIDE FOR THE PREVENTION OF POSTOPERATIVE PANCREATIC FISTULA

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Background: Resection remains the only definitive treatment of most benign and malignant tumors of the pancreas. Despite improved surgical techniques and perioperative management, 90-day mortality rates are as high as 7.4% and morbidity rates vary between 20 and 50%. Pancreatic fistula (PF) is regarded as the major source of morbidity and mortality following pancreatic resection, and affects 13–41% of patients. Efforts addressing the different methods of closure and anastomosis have failed to show significant superiority in decreasing PF incidence. Somatostatin analogues, however, have shown promising outcomes in prevention of PF through their inhibitory effects on pancreatic exocrine function. Lanreotide, (somatuline depot) a long-lasting depot formulation somatostatin analogue, is approved by FDA for the long-term treatment of acromegaly and advanced GEP-NETs, but there has been no prior experience using Lanreotide to decrease PF. Herein, we present our ongoing trial investigating Lanreotide for the prevention of postoperative pancreatic fistula.

Methods: This study is designed as a single arm Phase 2 trial. Our goal accrual is 98 evaluable patients who receive the study drug and undergo planned elective pancreaticoduodenectomy or distal pancreatectomy over a period of 36 months beginning February 2018. Patients receive a single dose of subcutaneous SOMATULINE DEPOT 120 mg immediately prior to operation and are followed for 60 days to assess for the presence of postoperative complications and study drug-related adverse events (AEs). The primary outcome is a composite of clinically significant PF (grade B or C) or intra-abdominal abscesses. Secondary outcomes include: postoperative surgical site infection, overall postoperative morbidity, drain amylase levels on postoperative days 1 and 3 and duration of drainage. The most common anticipated AEs of the drug include: diarrhea, abdominal pain, injection site reaction, nausea, vomiting, headache, lethargy, hyperglycemia and pancreatic insufficiency. Outcomes, at the end of study, will be compared to outcomes of historical controls matched on pancreatic firmness and duct size.

Results: Since study start, 42 patients have enrolled and 29 have completed the 60-day follow-up. Interim analysis was performed on the 29 patients who have completed the study. No mortalities were observed and no drug-related AEs were detected. The primary outcome did not occur among distal pancreatectomy patients (n=8). In the pancreaticoduodenectomy group (n=21), 3 patients met the study's primary end point. Two of these patients underwent re-operation and one patient had percutaneous drainage. As for secondary outcomes, surgical site infection developed in one patient, from the pancreaticoduodenectomy group. Overall postoperative morbidity was detected in 11 patients, including 2 patients from the distal pancreatectomy group who had grade A PF. Mean postoperative day 1 and day 3 drain amylase levels, including all of the patients were 2091 ± 4582 and 806 ± 2706 , respectively and median duration of drainage was 4 (3–20) days.

Conclusions: Our interim analysis including approximately one third of the goal number of patients, shows promising initial outcomes. If the final study results suggest clinically significant benefits to preoperative Lanreotide administration, a large-scale multicenter randomized controlled trial will be warranted.

GLOBAL BURDEN OF HAND TRAUMA: TRENDS OF FRACTURE AND DIGIT AMPUTATION, 1990–2017

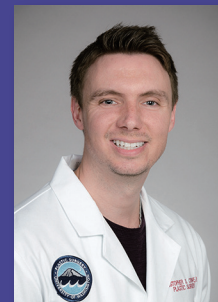
Crowe CS, Massenburg BB, Morrison SD, Naghavi M, Friedrich JB

Background: Injuries of the hand and wrist are frequent, and can be associated with chronic pain, lost productivity, and decreased quality of life. As global rates of mortality improve, rates of non-fatal injury increase, particularly in developing nations. Understanding global patterns of hand trauma over time can provide insight for improving preventative strategies.

Methods: The Global Burden of Diseases, Injuries, and Risk Factors Study 2017 (GBD 2017) was used to estimate prevalence, age-adjusted incidence, and years lived with disability (YLDs) for hand trauma in 195 countries from 1990 to 2017. Individual injuries included hand and wrist fractures, thumb amputations, and non-thumb digit amputations. Estimates of prevalence and incidence were derived from a previously described Bayesian meta-regression tool, DisMod-MR 2.1. YLDs were estimated from a prevalence estimate and disability weights for health states of each injury sequelae. Differences between males and females, countries, geographic regions, and Socio-demographic Index (SDI) were calculated. All estimates were computed with a 95% uncertainty interval (UI).

Results: The global incidence of hand trauma has decreased by approximately 3.5% worldwide since 1990. In 2017, the age-adjusted incidence of hand and wrist fractures was 179 per 100,000 (146 to 217), whereas the less common injuries of thumb and non-thumb digit amputation were 24 (17 to 34) and 56 (43 to 74) per 100,000, respectively. Rates of injury vary greatly by region and improvements have not been equally distributed. The highest burden of hand trauma persists in the high SDI group. Central Europe, Eastern Europe, and Australasia regions experience the highest rates of incidence and YLDs associated with hand trauma. Specifically, New Zealand, Czech Republic, Slovenia, Slovakia, Poland, and Australia are the primary contributors to this pattern. Changes in the incidence and YLDs of hand trauma, however, are unrelated to incidence and YLDs. The low-middle and middle SDI groups comprise countries with increasing rates of hand trauma. This corresponds to East Asia, the Caribbean, Oceania, and Tropical Latin America regions.

Conclusions: Hand trauma can lead to significant impairment, lost productivity, and decreased quality of life. Certain regions are noted to have persistently high rates of hand trauma and associated YLDs over the study period. These patterns, specifically high rates of injury in Central and Eastern Europe, are consistent with other anatomic zones of injury (e.g. facial fracture, traumatic brain injury, and spinal cord injury). It is hypothesized that these regions experience higher rates of non-fatal trauma, particularly in younger males. More concerning are low-middle and middle SDI countries, which have demonstrated increasing rates of fracture and amputation over the last 27 years, as patients in these countries are less likely to have access to quality and subspecialized surgical hand care. More work is required to understand the determinants of these injuries.



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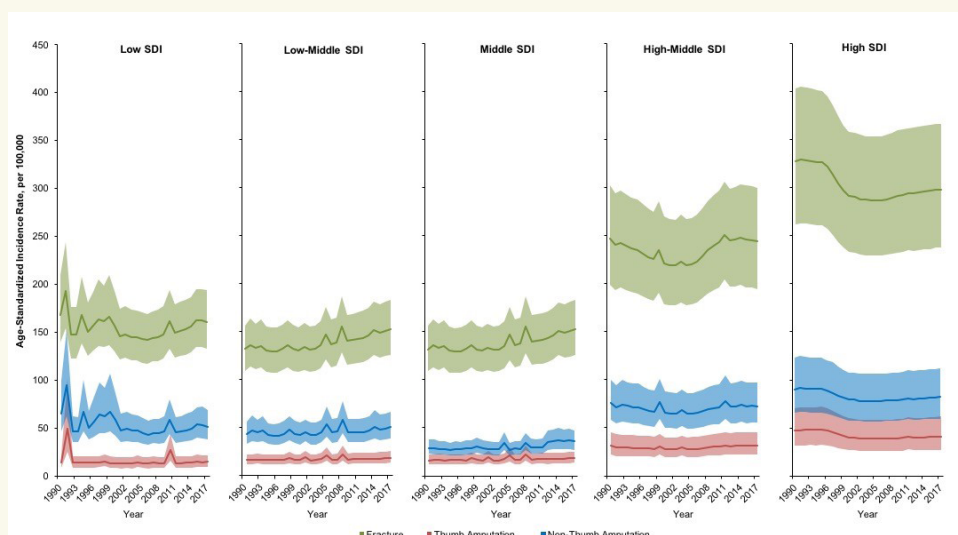
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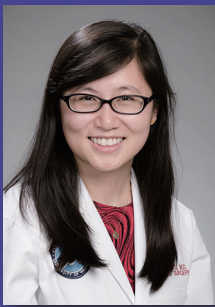
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MASTECTOMY WITH IMMEDIATE BREAST TISSUE EXPANDER RECONSTRUCTION: THE UNIVERSITY OF WASHINGTON EXPERIENCE

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Background: Mastectomy with immediate tissue expander placement is frequently performed for patients with breast cancer, including those with significant risk factors. This study identifies patients who underwent this procedure, assesses risk factors for early complication, and characterizes trends in postoperative management.

Methods: Patients who underwent immediate placement of a breast tissue expander (TE) placement for oncologic breast reconstruction at the University of Washington Medical Center between January 31, 2017, to January 31, 2018 were included in the study. Premorbid conditions, operative details, and postoperative management characteristics were obtained by retrospective chart review. Outcomes were assessed through 1 year following tissue expander placement or until the subsequent stage of breast reconstruction was performed. Median and interquartile ranges (IQR) were determined for each parameter.

Results: A total of 66 out of 99 patients met study inclusion criteria. The median length of stay was 27.1 hours (IQR 24.8–29.3 hours) with only five patients staying beyond one midnight. Ninety-four percent of patients received Exparel intercostal nerve blocks intraoperatively. The median morphine milligram equivalent for cumulative inpatient narcotic medication use was 30 mg (IQR 7.5–54.4 mg). The median number of tablets of narcotic pain medication prescribed at discharge was 60 (IQR 49–90) with 20% of patients receiving 100 tablets at discharge. Number of tablets at discharge was not correlated with inpatient opioid use (Pearson's correlation $r=0.30$, $p=0.813$). Only two patients required takeback to the OR within 24 hours of initial surgery, both for breast hematomas. One patient required postoperative ICU admission for hypotension due to secondary adrenal insufficiency. Eleven percent of patients visited the ED in the postoperative period. Within the first 30 days after surgery, 31.8% of patients experienced complications, and 15.2% of patients required antibiotics. Following 30 days postoperatively, 15.2% of patients experienced a complication. Eight patients required readmission postoperatively. Over the study period, 7.6% of patients underwent unexpected removal or replacement of their tissue expander.

Conclusions: Review of institutional data regarding immediate breast tissue expander placement reveals potential areas for improvement. The majority of patients undergoing mastectomy with immediate tissue expander placement are discharged on postoperative day one, and only two patients required takeback to the OR within 24 hours of the initial surgery. It is possible that those with low preoperative risk and uneventful intraoperative courses may discharge following recovery in the PACU. Furthermore, opioid prescription at discharge should be scrutinized as patients are prescribed varying amounts of narcotic pain medication without clear guidelines. Future work should be focused on understanding predictors for prolonged length of stay, as well as increased narcotic usage.

PATIENT REPRESENTATION IN PLASTIC SURGERY LITERATURE: ARE WE APPROPRIATELY DEPICTING DIVERSITY?

Cho DY, Kneib CJ, Crowe CS, Sobol DL, Morrison SD, Sousa JD

Background: Profound racial and ethnic disparities in the delivery, access, and appropriation of healthcare exist. Prior reports in plastic surgery have revealed disparities in the access of minority patients to breast reconstruction, replantation in hand injuries, and clinical trials. The aim of this study was to determine if published plastic surgery images accurately reflect racial demographics of patients undergoing plastic surgery procedures as well as the general population, both within the United States and globally.

Methods: A bibliometric analysis was performed on six leading journals in the field of plastic surgery: *Annals of Plastic Surgery* (APS), *Aesthetic Surgery Journal* (ASJ), *Journal of Craniofacial Surgery* (JCFS), *Journal of Hand Surgery* (JHS), *Journal of Plastic, Reconstructive, and Aesthetic Surgery* (JPRAS), and *Plastic and Reconstructive Surgery* (PRS). The *New England Journal of Medicine* (NEJM) *Images in Clinical Medicine* feature was included as a non-plastic surgery control. Journals were searched for color photographs and rendered graphics that contained depictions of human skin. The subject of each figure was categorized as “white” or “non-white” using the Fitzpatrick scale as a guide.

Results: 24,209 color photographs and 1,671 color rendered graphics were analyzed. 78% of photographs were of white patients, and 22% of photographs were of non-white patients. In plastic surgery journals, 22% of photographs were non-white and the average number of photographs per article with white skin was 5.4 compared to 1.6 with non-white skin ($p < 0.0001$). Similar results were seen in the NEJM (18% of photographs with non-white skin, average of 1.3 white versus 0.29 non-white skin, $p < 0.0001$). In plastic surgery journals, there was a significant increase in non-white photographs over time ($r = 0.086$, $p < 0.001$) and a significant association of non-white photographs with international articles ($r = 0.12$, $p < 0.001$). For comparison, 23% of the United States’ population is non-white while 30% of patients who seek cosmetic plastic surgery are non-white.

Conclusions: This is the first large-scale study to explicitly demonstrate the implicit racial biases that exist in the clinical images portrayed in medical publishing. Proportionally, the racial breakdown of medical photographs and graphics does not reflect the world population, the population of the United States, or the population of patients seeking plastic surgery with a significant bias towards “white” subjects. Studies published by authors from outside of the United States, were more likely to include non-white photographs. Biases in medical images persist in both plastic surgery and multidisciplinary journals. Such biases can contribute to inequalities in the delivery, access, and appropriation of healthcare.

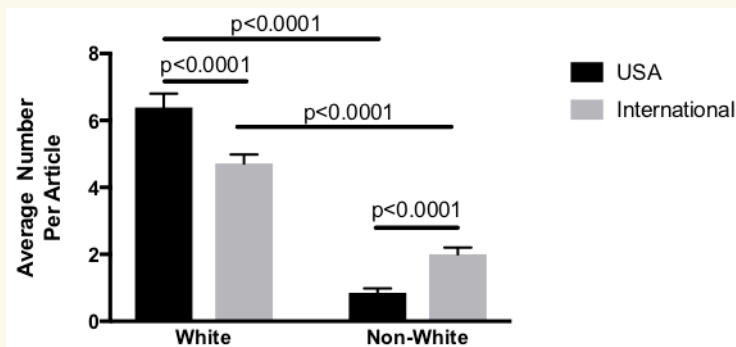
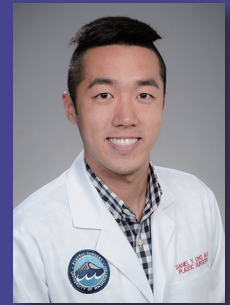


Figure 1 Average number of photographs per article for plastic surgery journals stratified by articles originating from the United States and internationally.



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Craniosynostosis,

Biomaterials, Drug Delivery,

Racial Equity in Healthcare



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Geriatric Trauma, Trauma
Systems Management, Triage

CHANGING THE SYSTOLIC BLOOD PRESSURE THRESHOLD FOR TRAUMA TEAM ACTIVATION IN OLDER ADULTS

Lisse GL, Butler EK, Mills BM, Glenn M, Cuschieri J, Arbabi S

Background: It has been suggested that the current physiologic field triage criteria have low predictive power for identifying significant injury in older adults, and that perhaps a systolic blood pressure (SBP) threshold of less than 110 mmHg for triage to a trauma center is appropriate for older adults, rather than the traditional SBP less than 90 mmHg. We seek to identify if there is an ideal pre-hospital or first emergency department (ED) SBP threshold to predict early mortality, shock, or the need for early intervention in older adult trauma patients.

Methods: This was a retrospective cohort study of 14,992 trauma patients presenting to Harborview Medical Center between January 1, 2012 and March 31, 2018. In order to determine the ideal SBP threshold, we used a composite endpoint of “early critical resource use” defined as: need for blood products, advanced airway management, angiography, or major operation within 4 hours of arrival or intracranial pressure monitoring or death within 24 hours of arrival. We also evaluated early mortality (defined as death in the hospital within the first 24 hours) and laboratory evidence of shock (defined as a base deficit ≥ 6 mEq/L or lactic acid ≥ 3 mmol/L). We performed a receiver operator curve analysis using the lowest blood pressure obtained in the field or in the ED. For each endpoint, we determined the current sensitivity for SBP < 90 mmHg. The ideal threshold for each decade age group was determined in order to maintain the current sensitivity.

Results: Using the current standard SBP < 90 mmHg, the overall under- and over-triage rates for the composite early resource use endpoint was 63.0% and 4.5%, respectively; there was no trend in SBP threshold by age group and the optimal cutoff for age ≥ 65 was 85 mmHg, with an under-triage rate of 59.7% and an over-triage rate of 5.3%. For early mortality, the current standard SBP < 90 mmHg has an under-triage rate of 29.9% and an over-triage rate of 9.7%. In order to maintain an under-triage rate of at most 30%, an increasing SBP threshold was required with each decade of life after 60 years and the optimal cutoff for age ≥ 65 was 109 mmHg, with a under-triage rate of 29.5% and over-triage rate of 35.2%. For laboratory evidence of shock, SBP < 90 mmHg has an under-triage rate of 54.4% and over-triage rate of 6.6%; there was no trend in SBP threshold by age group and for adults age ≥ 65 , the optimal SBP cutoff was 83 mmHg, with an under-triage rate of 50.4% and over-triage rate of 6.3%.

Conclusions: Modifying the systolic blood pressure parameter from the current standard 90 mmHg has implications for under- and over-triage rates of trauma patients who are at risk for early mortality, shock, and the need for early interventions. For adults age ≥ 65 , using SBP < 110 mmHg may be more appropriate for early mortality, however there does not appear to be an increase in shock in these patients. Regarding early intervention, the ideal SBP in adults age ≥ 65 was similar to that in younger adults. In adults age ≥ 65 , using an SBP < 100 mmHg may be ideal for identifying seriously injured trauma patients.

RADIATION SAFETY IN VASCULAR SURGERY TRAINING AND PRACTICE: A SURVEY OF EXPERIENCE AND EXPOSURE

Ohlsson, A, Singh, N, Shin, S

Background: Radiation exposure in interventional specialties presents a real and foreseeable health risk. Radiation safety education and practice is not standardized for physicians. We sought to evaluate radiation safety education and practices in vascular surgery (VS), interventional radiology (IR), and interventional cardiology (IC) in order to identify areas for improvement both in practice and establishing education during training.

Methods: A voluntary, anonymous survey was distributed to trainee and faculty members of the departments of VS, IR, and IC at a single institution with traditional fellowship (IR, IC, and VS) and integrated residency (VS only) training programs. Responses were collected and analyzed for trends, proportions, and free response answers.

Results: A total of 36 participants responded with a response rate of 78%. All participants agreed that radiation safety was important and reported having formal education in radiation safety. All participants reported wearing full body lead routinely when working with radiation. However only 81% of faculty and 80% of trainees reported routinely wearing leaded glasses and 86% of faculty and 93% of trainees routinely wore thyroid shields. Only 47% of participants reported always wearing a dosimeter while working with radiation and 13% reported never wearing it (Figures 1 and 2). Only 66% of participants reported turning dosimeters in monthly and 9% reported never turning them in. The most common barriers to dosimeters usage were inconvenience forgetting to wear them, and the lack of consequences for not wearing them.

Conclusions: Radiation safety education and practice is valued, however there is no standardization for safety practices and dosimeter use within our institution and across specialties. While protective lead is routinely used, monitoring of radiation exposure is not routine due to a variety of barriers.



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Research Interests
Dialysis Access, Tibial
Artery Interventions for CLI,
Radiation Safety

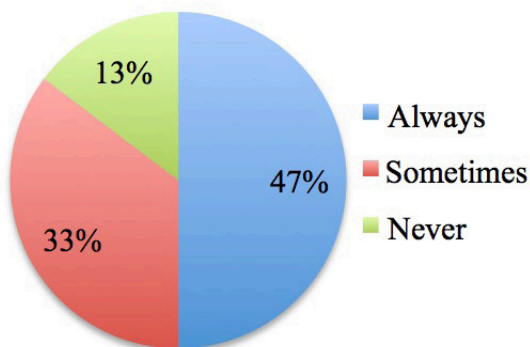


Figure 1. Frequency of Dosimeter Use

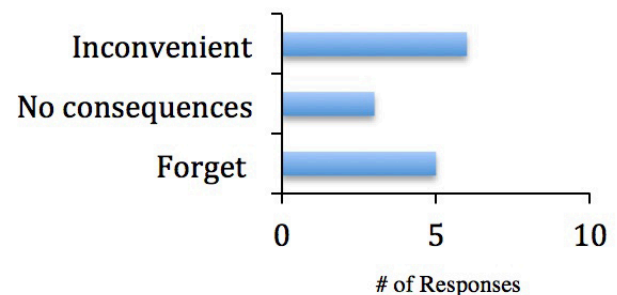


Figure 2. Barriers to Wearing a Dosimeter



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Process Improvement,
Education, PAD

PREVALENCE OF CHRONIC OPIOID USE IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE UNDERGOING LOWER EXTREMITY INTERVENTIONS

Ur R, Velazquez-Ramirez G, Krebs J, Stafford J, Craven TE, Bleyer A, Goldman MP, Hurie JB, Edwards MS

Background: Opiate use, dependence, and the associated morbidity and mortality are major current public health problems in the United States. Little is known about patterns of opioid use in patients with peripheral arterial disease (PAD). The purpose of this study was to identify the prevalence of chronic preoperative and postoperative prescription opioid use in patients with PAD. A secondary aim was to determine the demographic, comorbid conditions, and operative characteristics associated with chronic opioid use.

Methods: Using a single-institution database of patients with PAD undergoing open or endovascular lower extremity intervention from 2013–2014, data regarding opiate use and associated conditions were abstracted for analysis. Preoperative (PreCOU) and postoperative chronic opioid use (PostCOU) were defined as consistent opioid prescription filling in the three months before and after the index procedure, respectively. Opioid prescription filling was assessed using the North Carolina Controlled Substance Reporting System. Demographics, comorbid conditions, other adjunct pain medication data, and operative characteristics were abstracted from our institutional electronic medical record. Associations with PreCOU were evaluated using t-test, Wilcoxon test, or two sample median test (continuous), or chi-square or Fisher's exact test (categorical).

Results: 207 patients undergoing open or endovascular revascularization for claudication or critical limb ischemia were identified for analysis. Mean age was 64.8 years and 36% were female. Claudication was the indication for revascularization in 26% of patients and CLI was the indication in 74% of patients. Median preoperative ABI was 0.50. Seventy patients (34%) met the definition for PreCOU. PreCOU was associated with female gender, history of chronic musculoskeletal pain, benzodiazepine use, and self-reported illicit drug use. Less than 50% of patients reported use of non-opiate adjunct pain medications. No association was observed between PreCOU and pre or postoperative ABI, operative indication or number of prior lower extremity interventions. Following revascularization, median ABI was 0.88. PreCOU was not associated with significant differences in postoperative complications, length of stay, or mortality. Overall, 72 patients (35%) met the definition for PostCOU, 14 of whom had no history of preoperative chronic opiate use. Eleven patients with PreCOU did not demonstrate PostCOU.

Conclusions: Chronic opiate use was common in patients with PAD with a prevalence of approximately 35%, both prior to and following revascularization. Revascularization was associated with a termination of chronic opiate use in less than 20% of patients with PreCOU. Additionally, 10% of patients who did not use opiates chronically before their revascularization did so afterwards. Patients with PAD requiring intervention represent a high risk group with regards to chronic opiate use. Increased diligence in identifying opioid use among PAD patients and optimizing the use of non-narcotic adjunct pain medications may result in a lower prevalence of chronic opiate use and its attendant adverse effects.

EVALUATING THE ROLE OF HYPOXIA IN ANTI-TUMOR IMMUNE RESPONSES TO ADENOCARCINOMA

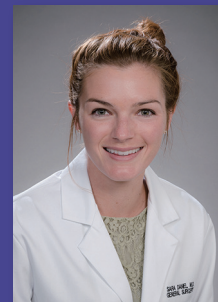
Daniel SK, Sullivan KM, Labadie KP, Kenerson HL,
Jiang X, Kim TS, Zhen DB, Pillarisetty VG

Background: Single agent immune checkpoint inhibition has not been found as effective in gastrointestinal solid tumors as in other malignancies. This is despite the presence of tumor infiltrating lymphocytes (TILs), including clonally expanded CD8⁺ cells in the tumor microenvironment (TME). Hypoxia is a known element of the TME that may influence the success of combination immunotherapies, although mechanisms of this effect are not fully elucidated. One proposed mechanism for the influence of hypoxia is through the induction of activated myofibroblast proliferation with resulting changes in stromal composition and chemokine production. Of particular interest is CXCL12, a chemokine which is thought to play a role in preventing cytotoxic T cell migration to tumor cells.

Methods: Fresh tumor cores obtained in the OR are sliced into 250 um discs and then cultured on a semipermeable membrane. The following day they are treated with plain media, IgG control, anti-programmed cell death antibody (anti-PD-1), CXCL12 inhibitor (AMD3100) with IgG, or AMD3100 with anti-PD-1. The slices are then either placed in a standard 20% O₂ (atmospheric) incubator or 2% O₂ (hypoxic incubator). After 48 hours of treatment in either condition, the slices are fixed in formalin or frozen for later RNA extraction.

Results: Three colorectal adenocarcinoma liver metastases (CRCLM), two pancreatic ductal adenocarcinomas (PDA), and one breast adenocarcinoma liver metastasis (BRLM) have been cultured in both atmospheric and hypoxic O₂ conditions. Based on cleaved-Caspase-3 (cC3) immunohistochemistry (IHC), no significant difference was found in overall cell apoptosis at atmospheric and hypoxic O₂ conditions in the BRLM and PDAs, however there was a significant decrease in cC3 staining in hypoxic compared to atmospheric O₂ in the CRCLM group (p=0.05). Whole slice RNA analysis was performed on one PDA sample with all the above treatment groups. Caspase 3, CXCL12, and CCL18 mRNA were all decreased in 2% O₂ compared to 20% while IL-6 mRNA was increased (all p<0.001).

Conclusions: Hypoxia in the tumor slice culture model affects expression of cytokines and chemokines. Further research needs to be done to understand the effects of hypoxia on responses to combination immunotherapy in solid tumors.



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Craniofacial Surgery, Plastic
Surgery, Global Health

UNDERSTANDING CHANGES IN THE GLOBAL BURDEN OF OROFACIAL CLEFTS FROM 1990 TO 2017

Massenburg BB, Crowe CS, Morrison SD, Alonso A,
Calis M, Donkor P, Kreshanti P, Yuan J, Hopper RA

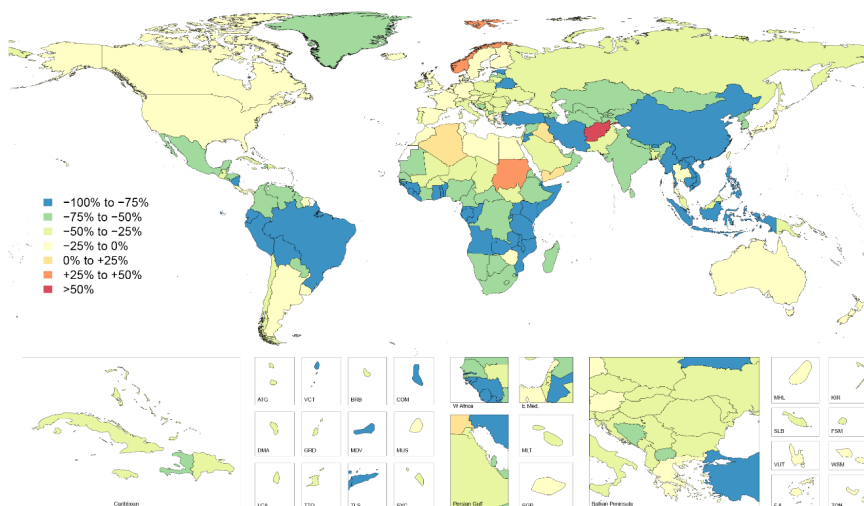
Background: Orofacial clefts are one of the most common congenital anomalies, but this disease burden is unevenly distributed worldwide. The objective of this study is to analyze the global patterns and morbidity of orofacial clefting.

Methods: The Global Burden of Disease methodology was used to estimate prevalence, disability adjusted life years (DALYs), and years lived with disability (YLDs) of orofacial clefting in 195 countries from 1990 to 2017. Linear regression was used for temporal and geographic analysis. Our international authorship hypothesizes on multiple factors contributing to this change based on their region's perspective.

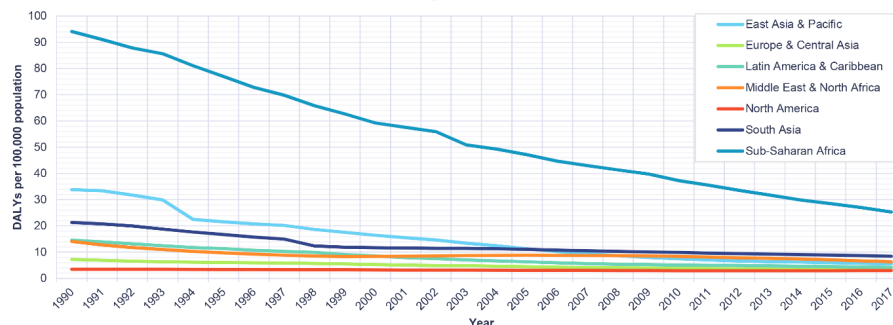
Results: From 1990 to 2017, the number of clefts worldwide decreased insignificantly by 4.9% to 10.8 million. The burden of this disease, however, significantly decreased to 652,084 DALYs (70.2% decrease) and 320,775 YLDs (12.5% decrease). Low- and middle-income countries experience 83.5% of the DALY burden. The largest decreases in DALY were seen in East Asia and the Pacific (83.6% decrease) and Sub-Saharan Africa (73.1% decrease), while North America (14.2% decrease) and high-income countries (20.5% decrease) remained neutral.

Conclusions: The burden of orofacial clefts has decreased significantly despite steady prevalence over the past 28 years. This study brings attention to patterns in disease burden, particularly the variance in morbidity between world regions. International craniofacial care has been improving over the past 25 years worldwide to reduce the burden on patients with orofacial clefts.

Relative Changes in Disability Adjusted Life Years for Orofacial Clefts in Both Sexes in 195 Countries or Territories From 1990 to 2017



Relative Changes in Disability Adjusted Life Years for Orofacial Clefts in Both Sexes in World Bank Regions from 1990 to 2017



A LEGISLATIVE FRAMEWORK TO ADDRESS CHEMICAL ASSAULT

Stewart BT, Kazerooni Y, Mishra B, Gibran N, Adu E, Clarke D, Pham T

Background: The incidence of chemical assault is increasing globally. However, there is no legislative framework or coordinated approach for controlling chemical assaults. To fill this gap, we aimed to develop a comprehensive legislative framework for advocacy groups and governments that might inform ways to control chemical assault.

Methods: Terms related to chemical assault were used to systematically search the academic, lay, and legal literatures (i.e., PubMed, World Health Organization Catalog, LexisNexis Academic, LexisNexis Advance, Google). Chemical assault was defined as the use of acid or another caustic or corrosive substance or vitriol by one person against another with the intent to injure or disfigure. Reports that described the use of chemical weapons in warfare were excluded. Data regarding the epidemiology of chemical assaults and pertinent legislation and the respective impacts of that legislation on chemical assaults were extracted. A secondary search of national legislations of countries with reports of chemical assaults was performed to construct a comprehensive legal framework based on existing laws and regulations using content analysis.

Results: After duplicates were removed, 2,366 records were screened for relevance. Most records (1,897 records) pertained to medical, surgical and psychosocial care of chemical injuries and were excluded. Of the remaining 470 reports, 384 met criteria for analysis. Chemical assaults were reported from 104 countries. From the laws and regulations of these countries, a framework consisting of 5 legislative priorities was developed: i) apply a public health approach; ii) adopt legal definitions specific to chemical assault; iii) control chemical supply, sales, and procurement; iv) facilitate justice; and v) support survivors. No country has implemented all of these legislative priorities.

Conclusions: The comprehensive legislative framework can be used to coordinate existing chemical assault control efforts. Advocacy groups and governments might consider implementation and enforcement of the legislative framework to control the growing epidemic of chemical assault. Comparative policy analysis and assessments of the impacts of new and/or additional legislative efforts may further inform strategies to prevent, prosecute, and mitigate the impact of chemical assaults.

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Research Interests

International Injury and
Burn Control; Health
Disparities and Equity



Apply a public health approach

- Deploy awareness campaigns regarding laws and stigma
- Include gender empowerment and equity into education curricula
- Establish passive and active surveillance systems



Adopt definitions specific to chemical assault

- Clarify language beyond assault, (attempted) murder, or domestic violence
- Recognize chemical assault as a form of gender-based violence
- Classify caustic and corrosive substances and vitriol as weapons



Control supply, sales, and procurement

- Enforce international laws regarding management of hazardous substances
- License chemical sellers
- Maintain a registry of chemical sellers and purchasers
- Criminalize purchase and possession of chemicals with intent to harm



Facilitate justice

- Empower and mandate local law enforcement investigations of chemical assault
- Define minimum sentences for chemical assault
- Create special tribunals for trials of chemical assaults
- Provide protection and legal aid for survivors



Support survivors

- Provide free and life-long medical and psychological care and rehabilitation
- Build comprehensive burn care capacity
- Provide recompense and opportunities for education and employment
- Foster coalitions and partnerships to support survivors



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Research Interests

Surgical Education

A LOW-COST SIMULATION MODEL AND INSTRUCTIONAL VIDEO FOR ESCHAROTOMY TRAINING

Thomas M, Curtis E, Stewart B, Mandell S, Pham T

Background: In the acute management of deep circumferential or near-circumferential burns of the extremities and chest, escharotomy is the only effective surgical intervention to alleviate impending vascular compromise and relieve chest constriction. In resource-limited environments such as low- and middle-income countries (LMIC) and military deployments where evacuation may be delayed, prior training in the proper performance of escharotomy is essential as this is both an infrequent and high-risk procedure. The objective of this study was to validate a previously described escharotomy model and examine whether it enhanced self-efficacy, knowledge and skill of medical personnel.

Methods: In-hospital and pre-hospital medical personnel, with varying degrees of burn care-related experience, participated in a one-hour training session. The first portion consisted of an introductory video presentation describing the indications, preparation, steps, pitfalls and complications associated with escharotomy. The second part of the training consisted of a supervised hands-on simulation with a low-cost (\$75 supply cost plus manikin) and low-fidelity escharotomy model (figure 1). Students were then queried using a psychometrically validated student learning and self-confidence in simulation questionnaire (National League of Nursing, 2003). The questions focused specifically on simulation design, knowledge, active learning and realism.

Results: Twenty-two participants were grouped according to burn experience: burn attending physicians (4), general surgery residents (9), medical students (6), and pre-hospital personnel (3). Ninety percent of participants (20/22) thought their self-efficacy to perform and understand the role of an escharotomy was enhanced. Ninety-five percent of participants (21/22) reported that the teaching model provided an interactive learning opportunity that simulated a real-life scenario.

Conclusions: Simulation training using this low-fidelity model allowed acquisition of necessary skills to simulate an escharotomy. This teaching model is easily reproducible, cost effective and can be used to increase the self-efficacy, competency and knowledge of medical personnel before they are called to perform actual escharotomy procedures.

Applicability of Research to Practice: Studies to validate low-cost, low-fidelity simulation strategy are necessary to target burn care training in resource-limited environments.

Figure 1



IMPROVING OPERATING ROOM EFFICIENCY: A MACHINE LEARNING APPROACH TO PREDICT CASE-TIME DURATION

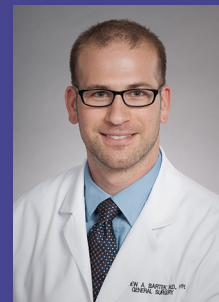
Bartek MA, Saxena RC, Solomon S, Fong CT,
Behara LD, Venigandla R, Nair BG, Lang JD

Background: Optimizing operating room (OR) utilization is vital for delivering high quality and efficient care. Current methods of estimating case duration include surgeons' own estimates and electronic medical record (EMR) estimations based on historic averages at surgeon and procedure levels. These methods yield inaccurate estimates, leading to inefficiencies, delays, and overtime costs. Our objective was to develop statistical models in a large retrospective dataset to improve estimation of case-time duration relative to current standards.

Methods: We developed models to predict case-time duration using two different methods: linear regression and supervised machine learning, using Extreme Gradient Boosting (XGBoost) and random forest algorithms for the latter. For each of these models, we generated: 1) service-specific models and 2) surgeon-specific models in which surgeons were modeled individually. Our dataset included 46,986 scheduled surgeries performed at our center from January 2014 to December 2017, with 80% used for training and 20% for model testing/validation. Predictions derived from each model were compared to estimations based on historic averages and to predictions by the surgeon, our institutional standard. Models were evaluated based on accuracy, overage (where actual case duration > predicted + 10% tolerance threshold), underage (actual case duration < predicted - 10% tolerance threshold), and the predictive capability of being within a 10% tolerance threshold.

Results: The XGBoost ML algorithm resulted in the highest predictive capability, with the linear model having the least. The surgeon-specific model was superior to the service-specific model, with higher accuracies, lower percentage of overage and underage, and higher percentage of cases within the 10% threshold. Notably, the ability to predict cases within 10% improved from 32% for the surgeon estimate or 30% by the historical average estimate to 39% with the XGBoost ML surgeon-specific model. In the analysis of the weighted importance of predictor variables, the majority of the information utilized in the models was based on procedure and personnel data. Overall, patient health metrics had a much smaller role compared to personnel or procedure factors in predicting case duration.

Conclusions: Our study is a notable advancement towards statistical modeling of case-time duration across all surgical departments in a large tertiary medical center. Machine learning approaches may improve case duration estimations, enabling improved OR scheduling, efficiency, and reduced costs.



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Research Interests
Surgical Decision Making

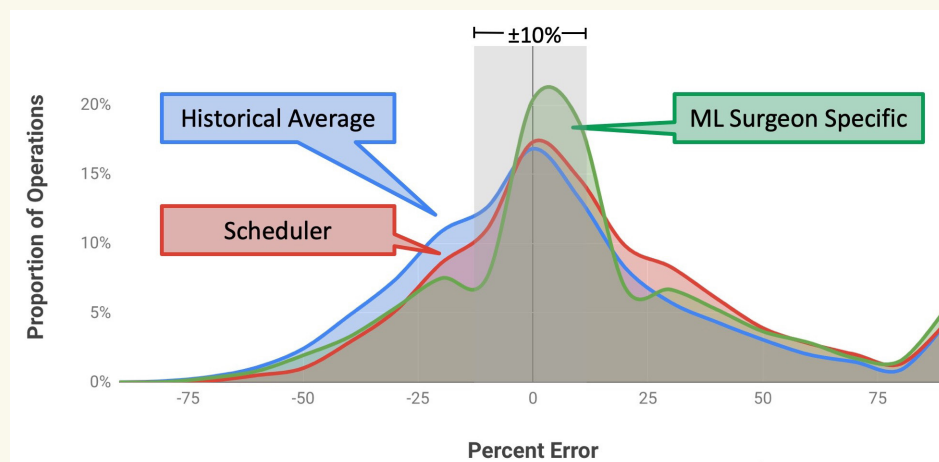
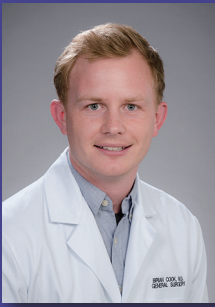


Figure 1: Distribution of prediction error



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Research Interests
Transplant Outcomes

CROSSMATCHES, DONOR-SPECIFIC ANTIBODIES AND ANTIBODY-MEDIATED REJECTION IN LIVER TRANSPLANT RECIPIENTS

Cook B, Perkins J, Warner P, Reyes J, Montenovio M, Kling C

Background: Immunologic rejection in liver transplantation has mostly been described by cellular mechanisms, but there has been recent interest in understanding antibody-mediated rejection (AMR). We sought to examine the role of donor-specific antibodies (DSA) in the development of AMR in liver transplant recipients.

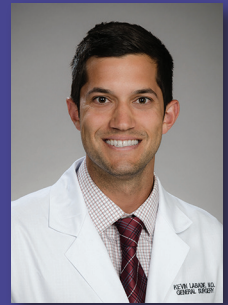
Methods: Flow cytometric crossmatches against donor lymphocytes were performed on all adult deceased donor liver transplant recipients at one center over a 22-month period. All positive crossmatches were then tested for DSA by single-antigen beads. The clinical course of patients who developed AMR is described.

Results: Of 148 liver transplant recipients, 114 (77.0%) had negative and 34 (22.9%) had positive crossmatches. Of recipients with a positive crossmatch, DSA were classified as strong (12/34, 35.3%), moderate (9/34, 26.4%), weak (4/34, 11.8%), or none (9/34, 26.4%). Compared to those with a negative crossmatch, a positive crossmatch was associated with female recipient gender (73.5 % vs 25.4%, $p<0.0001$) and higher MELD score (33.6 ± 5.8 vs 29.8 ± 6.5 , $p=0.002$). Three patients (2.0%) developed AMR – 2 (5.9%) with a positive crossmatch and moderate DSA and 1 (0.9%) with a negative crossmatch and medication non-compliance ($p=0.069$). Diagnosis of AMR was made with laboratory signs of hepatocellular injury, biopsy, and presence of DSA. Two cases of AMR were treated with plasmapheresis, IVIG and rituximab and 1 was managed with plasmapheresis and IVIG alone. At median follow up of 16.3 months (15.6–16.3 mo), graft function is normal in all 3 patients.

Conclusions: AMR is uncommon in liver transplant recipients, with a trend to being more common in recipients with a positive crossmatch.

ADOPTIVE TRANSFER OF GENETICALLY ENGINEERED MACROPHAGES TO REINVIGORATE ENDOGENOUS T CELL RESPONSES AGAINST ADVANCED GASTROINTESTINAL CANCER

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Translation of Novel Diagnostic and Therapeutic Modalities in Oncology

Background: Advanced gastrointestinal (GI) cancers, such as pancreatic and colorectal cancer, are associated with poor prognosis and are rarely cured with conventional chemotherapy. Multiple mechanisms exist by which these tumors diminish physiologic antitumor immune responses, including hijacking of immunosuppressive cellular elements and direct suppression of T cells. In efforts to reactivate TIL, genetically engineered macrophages (GEMs) were developed to secrete interleukin-12, a potent T-cell stimulating factor. Here we investigated the feasibility and efficacy of IL-12 producing GEMs (IL-12 GEMs) to increase tumor cell death in human GI solid tumor slice culture model.

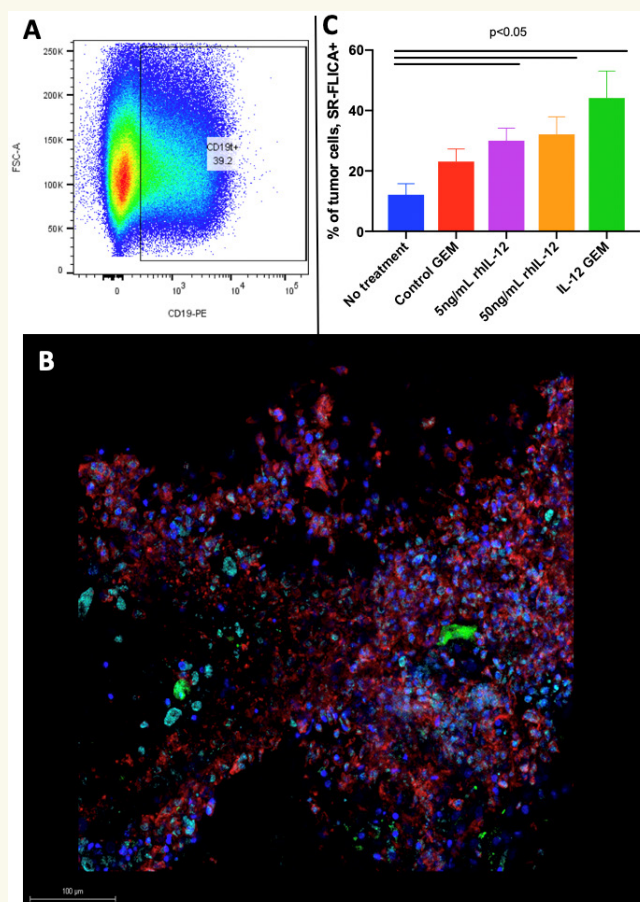
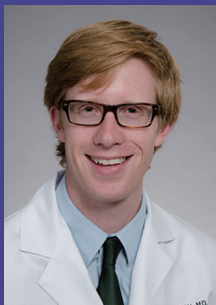


Figure 1 – IL-12 GEMs persist in tumor slice culture and increase tumor cell death by day 7. (A) Flow cytometry demonstrating 39.2% transduction of CD19t-T2A-hIL12 vector. (B) Representative confocal microscopic image of all nuclei (blue), tumor cells (red), IL-12 GEMs (green) and SR-FLICA (cyan) at day 7. (C) Percent of apoptotic tumor cells at day 6 (n = 4 high-power fields/group)

Methods: CD14⁺ monocytes were isolated from thawed healthy donor peripheral blood mononuclear cells and differentiated into macrophages using granulocyte-macrophage colony stimulating factor. Macrophages were transduced with epHIV7.2 CD19t-T2A-hIL12 or epHIV7.2 CD19t lentivirus to create IL-12 and control GEMs, respectively. For human tumor slice culture, 6mm punch biopsies were obtained from resected colorectal liver metastasis and a vibratome was used to create 250 μ m thick slices which were placed in individual culture wells. After one day in culture, 100,000 GEMs (control or IL-12), 5ng/mL or 50ng/mL of recombinant human IL-12 (rhIL-12) were added to each experimental group. GEMs and tumor cells were visualized with a Leica confocal microscope. Apoptosis was measured by fluorescent staining of activated caspase enzymes with SR-FLICA poly caspase assay kit.

Results: Allogenic GEMs were transduced with 39% efficiency of epHIV7.2 CD19t-T2A-hIL12 (Figure 1A). Control and IL-12 GEMs penetrated tumor slices and persisted for at least 7 days (Figure 1B). At day 6, IL-12 GEMs increased tumor cell death with 44% apoptotic tumor cells compared to 12% and 23% apoptotic tumor cells in the no treatment control (p=0.01) and control GEM groups (p=0.07). rhIL-12 increased tumor cell death with 30% and 33% apoptotic tumor cells in 5ng/mL and 50ng/mL treatment groups, respectively (Figure 1C).

Conclusions: IL-12 GEMs penetrate into tumor slices and drive anti-tumor activity.



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IL-10 BLOCKADE REACTIVATES ANTI-TUMOR IMMUNITY IN HUMAN COLORECTAL CANCER LIVER METASTASES

Sullivan KM, Jiang X, Seo YD, Kenerson HL, Yan X, Lausted C, Meng C, Jabbari N, Labadie KP, Daniel SK, Tian Q, Kim TS, Yeung TS, Pillarisetty VG

Background: Colorectal cancer (CRC) is the 4th most common cancer in the US, and the liver is the most common site of metastatic disease. Immune checkpoint inhibitor therapy has not been successful in achieving a clinical response in most patients with CRC liver metastases (CRCLM). The liver is known to induce tolerance to foreign antigens as a result of immunosuppressive cytokines including IL-10. We hypothesized that blockade of IL-10 signaling in CRCLM would potentiate tumor infiltrating lymphocyte (TIL)-mediated tumor cell death.

Methods: We performed single-cell RNA sequencing (scRNAseq) of CRCLM using the 10x platform to evaluate for expression of IL-10 or IL-10 receptor (IL-10R) RNA within the tumor (n=8). To confirm if the IL-10R protein was present within the tumor microenvironment (TME), we also performed immunohistochemistry (IHC) (n=3). In order to study the functional effects of IL-10 blockade, we utilized a tumor slice culture (TSC) model, which allows for the study of cancers with their intact TME including immune cells. For TSCs, cores (6 mm diameter) were taken from freshly resected sterile human CRCLM and cut to 250 μ m thick slices using a vibratome (n=3). Duplicate slices were treated with either IgG control or anti-IL-10 monoclonal antibodies and cultured for up to 6 days. To evaluate for histological evidence of necrosis and cell apoptosis within the tumor slice, we stained slides with either hematoxylin and eosin (H&E) or cleaved-Caspase-3 (CC3). To gain insight into the activation state of TIL after treatment, we measured levels of cytokines within the culture supernatants.

Results: We found by scRNAseq that IL-10 was expressed by a subset of tumor-associated macrophages, and IL-10R was expressed by both CD4⁺ and CD8⁺ T cells as well as macrophages. We confirmed that IL-10R protein was present within the CRCLM TME by IHC, and IL-10R expression was distributed throughout the stroma in non-tumor cells. In TSC treated with anti-IL-10 antibody, CC3⁺ cells were found to be 82.8% of total cells, compared to 36.1% of control ($p = 1 \times 10^{-6}$) at day 6. These findings were consistent across all human tumor samples treated with IL-10 blockade versus control at all time points examined. Furthermore, IL-10 blockade led to histologic evidence of generalized necrosis compared to an intact TME seen in the control group. Analysis of cytokines released into the media confirmed that IL-10 was present in controls, but absent in slices blocked with anti-IL-10 antibody. We also found increased levels of granzyme B, IL-2, GM-CSF, and IL-18, as well as a reduction in the immune checkpoint receptor TIM3, after one day of IL-10 blockade in culture.

Conclusions: Treatment of human CRCLM TSCs with anti-IL-10 antibody leads to a marked increase in immune-mediated cell death within the tumor. Our data suggest that IL-10 serves as a critical regulator of anti-tumor immunity in the CRCLM TME and may serve as an important immunotherapeutic target.

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The Helen and John Schilling Lecture is an annual lecture 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.

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