

UW Medicine

DEPARTMENT OF SURGERY

Presents

**The Eighteenth Annual
Research Symposium**

Friday, January 27, 2012
7:00 a.m. – 2:45 p.m.

Museum of History and Industry
McEachern Auditorium
2700 24th Avenue East
Seattle, Washington 98112

SCHEDULE OF PRESENTATIONS

Moderators: Gerald Fried, M.D. and David Flum, M.D.

7:00am	Introduction	Carlos Pellegrini, M.D. and David Flum, M.D.
7:15am	Kohler	Using the Health Belief Model to Develop Peri-Operative Parent Education Videos
7:30am	Sanchez	The Effect of Lipid Minimization on the Prevention of Parenteral Nutrition - Associated Cholestasis in Surgical Infants
7:45am	Auyang	Laparoscopic Lumbar Hernia Repair
8:00am	Kwon	Importance of Perioperative Glycemic Control in General Surgery: A Report from the Surgical Care and Outcomes Assessment Program
8:15am	Sham	Focal Nesidioblastosis in Adults: A Distinct Pathologic Entity Mimicking Insulinoma
8:30am	Overview	Michael Mulligan, M.D.
8:40am	Karamlou	Increased ECMO Center and Case Volume Are Associated with Improved ECMO Survival
8:55am	O'Kelly-Priddy	Extracorporeal Membrane Oxygenation Preserves Myocardial Protein Synthesis Without Altering Leucine Oxidation in Immature Swine In Vivo
9:10am	BREAK	
9:25am	Phelan	Toll-Like Receptor 4 Mediated Lung Ischemia-Reperfusion Injury: Signaling Beyond MYD88 and TIRAP
9:40am	Hayanga	Lung Cancer Mortality and Residential Segregation in the United States
9:55am	Overview	Saman Arbabi, M.D.
10:05am	Chung	Effect of Topical Mapk Inhibition on Hypertrophic Scarring in a Duroc Porcine Model
10:20am	Chang	Transplantation of Vascularized Composite Allografts in a Mismatched Setting Without the Need for Chronic Immunosuppression
10:35am	Thompson	Toll-Like 1 Receptor Polymorphisms and Associations with Outcomes in Sepsis Following Traumatic Injury
10:50am	Overview	Eileen Bulger, M.D.
11:00am	Garland	Alveolar Dead Space Correlates with Early Mortality in Trauma Patients
11:15am	Gage	Compliance with CDC Field Triage Guidelines in an Established Trauma System
11:30am	Park	Mortality Associated with Gram Negative Bacteremia May Reflect Early Alterations in Innate Immunity After Severe Traumatic Injury
11:45am	LUNCH	
12:30pm	Overview	Alexander Clowes, M.D.
12:40pm	Wallace	Intravascular Ultrasound: A Critical Tool for Accurate Endograft Sizing in Blunt Traumatic Aortic Injury
12:55pm	Jayaraj	Impact of Graduated Compressive Stockings on the Prevention of Post Thrombotic Syndrome: Results of a Randomized Trial
1:10pm	Overview	Raymond Yeung, M.D.
1:20pm	McAteer	Patient-Level Factors Associated with Antireflux Procedures in Children Hospitalized with Gastroesophageal Reflux Disease
1:35pm	Prucz	Cost-Effective Microsimulation Model of Negative Pressure Wound Therapy versus Standard Dressing in Acute Post-Surgical Wounds
1:50pm	Loviscek	The Medium Term Outcomes of Barrett's Esophagus in Patients Treated with Laparoscopic Anti-Reflux Surgery
2:05pm	Drake	The ACGME Caselogs: Changes Over Two Decades
2:20pm	Hinojosa	Outcomes of Nissen Fundoplication in Patients with Concurrent Idiopathic Pulmonary Fibrosis and Gastroesophageal Reflux
2:35pm	Closing	Carlos Pellegrini, M.D.
4:00pm	HELEN & JOHN SCHILLING LECTURE – Hogness Auditorium, UW HSB <i>Teaching Johnny How to Operate: Answering the "Bell"</i>	

Gerald Fried, M.D.
Adair Family Professor
Chair, Department of Surgery
Surgeon-in-Chief
McGill University Health Centre; Montreal, Quebec

USING THE HEALTH BELIEF MODEL TO DEVELOP PERI-OPERATIVE PARENT EDUCATION VIDEOS

Kohler J, Quiqley S, Buchmiller T, Weldon C, O'Donnell E, Fishman S

Purpose: Parents of children who require operations suffer from profound anxiety, which can impede their ability to understand and participate in their child's care. Informational videos have been shown to have an anxiolytic effect, as have empathic messages from other parents who have faced similar challenges. While several videos exist to address parental concerns surrounding common pediatric surgical conditions that require parental participation, including ostomies and central lines, there are few examples of a combined informative and empathic approach to parent education in pediatric surgery. We used a theory-grounded approach centered on the Health Belief Model (HBM) to develop a series of educational and anxiolytic videos for parents of children with ostomies and Port-a-cath central venous catheters. The Health Belief Model (HBM) provides a powerful theoretical basis for encouraging health behaviors in parents, by defining a series of constructs for behavior change: self-efficacy, perceived barriers, perceived benefits, perceived susceptibility, and perceived severity.

Methods: Pre-production research included a review of the literature, one-on-one and group interviews with key stakeholders, including attending surgeons, nurse practitioners, and ward nurses, and in-depth one-on-one interviews with 10 parents whose children had central lines or ostomies. Responses were analyzed to identify the effects of each construct of the HBM on parents' ability and willingness to participate in central line or ostomy care. Video production used the results of these interviews to develop a series of short online videos to decrease perceived barriers and severity while augmenting perceived benefits and susceptibility to encourage parents to assume control of their child's stoma or central line.

Results: Stakeholders identified a number of technical points that they felt needed to be reinforced or clarified for parents. Parents, in turn, identified peer support from other parents as something they would be eager to see in a video education tool. Fellow parents who have successfully coped with similar diagnoses and procedures are seen as being more definitive resources for emotional support and reassurance than professional providers. While most health communication campaigns focus on reducing perceptions of severity, parents in this study had unrealistically severe expectations about the risks and difficulty of caring for ostomies and Port-a-caths. These observations allowed us to create a series of videos using HBM theory to address all of these concerns.

Conclusions: The HBM is an effective theoretical framework for developing parent educational videos. The synergies of a combined message, incorporating both technical information from providers and emotional support messages from peers, has the potential to decrease the extremely high perceived severity associated with any childhood disease requiring surgery, and in so doing increase self-efficacy. On-line videos consisting of a number of short segments are the preferred method of delivery.

THE EFFECT OF LIPID MINIMIZATION ON THE PREVENTION OF PARENTERAL NUTRITION-ASSOCIATED CHOLESTASIS IN SURGICAL INFANTS

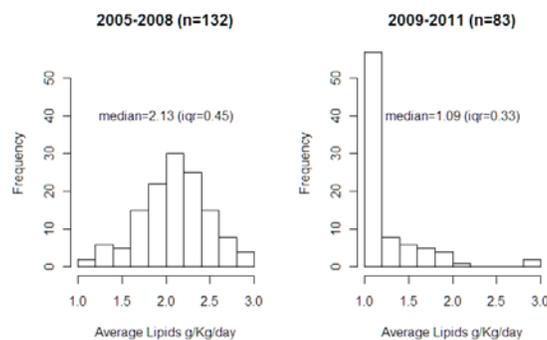
Sanchez S, Braun L, Mercer L, Javid P

Purpose: Surgical infants requiring long-term parenteral nutrition (PN) are at risk for parenteral nutrition-associated liver disease (PNALD). The purpose of this study was to determine the effect of a lipid minimized PN regimen in preventing PNALD in surgical infants. We hypothesized that lipid minimization would be associated with a lower incidence of PNALD in this population.

Methods: We conducted a retrospective review of surgical infants treated for necrotizing enterocolitis, gastroschisis and jejunoileal atresia at a single institution from June 2005 to July 2011 (IRB# 13654). Beginning in 2009, a lipid minimization strategy was implemented with a goal lipid provision of 1 g/kg/day throughout a patient's entire PN course. An experimental cohort of infants treated with lipid minimization from 2009-2011 (n=83) was compared to a control cohort of infants from 2005-2008 receiving standard intravenous lipid dosing (n=132). A multivariable relative risk regression model was constructed analyzing the association between lipid minimization and PNALD. Statistical significance was set at $p \leq 0.05$.

Results: Patients admitted during the lipid minimization era had reduced daily intravenous lipid provisions compared to the control group ($p < 0.001$, Figure 1). On univariate analysis, there were no differences in demographic or clinical characteristics between the two groups. A significant reduction in the incidence of PNALD was demonstrated in the experimental group compared to the control group (22% vs. 43%, $p = 0.002$). On relative risk regression, after controlling for gestational age, diagnosis, PN duration, and sepsis, patients treated with standard lipid provisions were 1.73 times more likely to develop PNALD than patients who were lipid minimized (95% CI: 1.14-2.63; $p = 0.01$).

Conclusion: Lipid minimization in surgical infants on long-term parenteral nutrition is associated with a reduction in the incidence of cholestatic liver disease. Early lipid minimization should be considered in all surgical infants who require parenteral nutrition as a preventative measure against parenteral nutrition-associated liver disease.

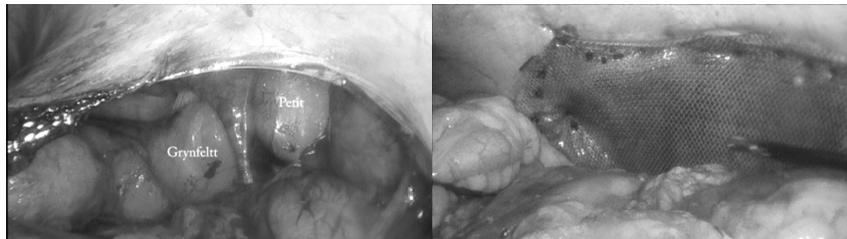


LAPAROSCOPIC LUMBAR HERNIA REPAIR

Auyang E, Wright A

Introduction: Lumbar hernias are rare clinical entities with less than 400 reported in the literature. They were first described by deGarangeor in 1731. Petit later characterized the inferior lumbar triangle hernia in 1783 and Grynfeltt the superior lumbar triangle hernia in 1866. 80% of lumbar hernias are acquired due to increased intra-abdominal pressure, surgical incisions, or trauma. The remaining 20% are congenital. There is a 25% risk of incarceration and >8% chance of strangulation associated with lumbar hernias. Therefore, repair is recommended for symptomatic hernias. Laparoscopic repair was first described in 1997. The laparoscopic approach has the advantage over an open approach due to better hernia defect visualization and more accurate hernia size measurement. An adequate underlay mesh can then be placed. We have completed 3 laparoscopic lumbar hernias. In this paper, we demonstrate a laparoscopic repair of a left-sided lumbar hernia (combined Petit and Grynfeltt) in a 47 year old male patient with a previous history of a motor vehicle accident.

Methods: The patient is placed in a 45 degree semi-lateral position. Insufflation is obtained using a Veress needle at a left peri-umbilical location. An 11-mm port is placed at this location and a 10-mm 30-degree angled laparoscope is used for visualization. Three additional working ports are placed for medial mobilization of the colon and kidney, reduction of the hernia, dissection of the hernia margins, and placement of an underlay mesh. A coated polyester mesh is placed with a 4-cm overlap in each direction. Trans-abdominal sutures are placed to anchor the mesh and laparoscopic tacks are used to circumferentially affix the mesh.



Results: The procedure was completed in 125 minutes with minimal blood loss and no intraoperative or postoperative complications.

Conclusion: Laparoscopic lumbar hernia repair is a feasible operation that provides excellent visualization and measurement of the hernia defect, and allows for application of an underlay mesh with adequate overlap.

IMPORTANCE OF PERIOPERATIVE GLYCEMIC CONTROL IN GENERAL SURGERY: A REPORT FROM THE SURGICAL CARE AND OUTCOMES ASSESSMENT PROGRAM

Kwon S, Thompson R, Dellinger P, Yanez D, Farrohki E, Rogers T, Flum D

Background: There is limited evidence to characterize the impact of perioperative hyperglycemia and insulin administration on adverse outcomes in patients, with and without diabetes, undergoing general surgical procedures.

Methods: The Surgical Care and Outcomes Assessment Program is a Washington State quality improvement benchmarking-based initiative. We evaluated the relationship of perioperative hyperglycemia (>180 mg/dL) and insulin administration on mortality, operative interventions, and infections for patients undergoing elective colorectal and bariatric surgery at 47 participating hospitals between 4th quarter of 2005 and 4th quarter of 2010.

Results: Of the 11,633 patients (55.4±15.3 yrs.; 65.7% women) with a serum glucose determination either on the day of surgery, postoperative day (POD) 1, or POD 2, 29.1% of patients were hyperglycemic. After controlling for patient and clinical factors, those with hyperglycemia had a significantly increased risk of infection (OR 2.0; 95% CI 1.63-2.44), reoperative interventions (OR 1.8; 95% CI 1.41-2.3), and mortality (OR 2.71; 95% CI 1.72-4.28). Increased risk of poor outcomes was observed both for patients with and without diabetes. Those with hyperglycemia on the day of surgery who received insulin had no significant increase in infections (OR 1.01; 95% CI 0.72-1.42), reoperative interventions (OR 1.29; 95% CI 0.89-1.89), or deaths (OR 1.21; 95% CI 0.61-2.42).

Conclusions: Perioperative hyperglycemia was associated with adverse outcomes in general surgery patients with and without diabetes. However, patients with hyperglycemia who received insulin were at no greater risk than those with normal blood glucoses. Perioperative glucose evaluation and insulin administration in patients with hyperglycemia are important quality targets.

FOCAL NESIDIOBLASTOSIS IN ADULTS: A DISTINCT PATHOLOGIC ENTITY MIMICKING INSULINOMA

Sham J, Park J, Mann G

Introduction: Almost all patients presenting with hyperinsulinemic hypoglycemia and a discrete pancreatic mass have an insulinoma. Diffuse nesidioblastosis is a well-described entity which can also present as hyperinsulinemic hypoglycemia and is characterized by dysplastic proliferation of pancreatic islet cells, scattered enlargement of beta-cell aggregates budding from ducts, and prominent cell nuclei. Although nesidioblastosis as a focal process has been previously described in infants younger than 7 months, only a handful of adult cases have been reported in the literature. We present three cases of focal nesidioblastosis in adults, the largest case series reported in the literature to date.

Cases: Two women and one man, ages 18-53, presented to their primary care provider with symptoms of hypoglycemia. Patients had either low post-prandial or fasting glucose levels. All three had either elevated fasting insulin (21-57microIU/ml, nl<17) or pro-insulin (35-46pmol/ml, nl<20) levels, while two had a documented rise in C-peptide levels (6.3-8.3ng/ml, nl<5). Cross sectional imaging revealed discrete pancreatic masses (0.6, 1.7cm) in two patients. Two patients underwent distal pancreatectomy while one underwent enucleation as surgical treatment for their condition. Pathologic review of all three specimens demonstrated focal nesidioblastosis. Hypoglycemia resolved in all three patients after surgery.

Discussion: Focal nesidioblastosis is an uncommon although distinct pathologic entity in adults which can present as hypoglycemia and a pancreatic mass. While the histologic distinction from insulinoma is clear, more investigation into the genetic and biochemical differences between the two processes is needed, as well as a better understanding of the natural history of this unique disease entity.

INCREASED ECMO CENTER AND CASE VOLUME ARE ASSOCIATED WITH IMPROVED ECMO SURVIVAL

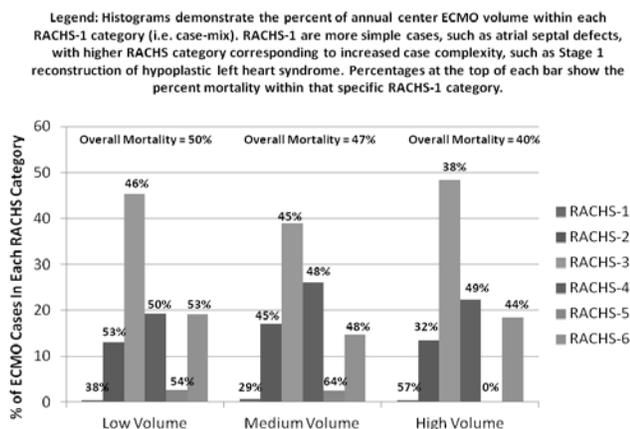
Karamlou T, Vafaezadeh M, Permut L, Cohen G, McMullan M

Background: Evidence supports a beneficial impact of higher center case volume on pediatric cardiothoracic surgical mortality. However, the influence of ECMO center case volume on pediatric patient survival is unknown. We sought to examine the relationship between ECMO case volume on survival in pediatric patients who require ECMO support.

Methods: Pediatric patients (age < 18 years) undergoing ECMO cannulation were retrospectively identified using the Healthcare Cost and Utilization Project (H-CUP) Kids' Inpatient Database (KID)- (years 2000, 2003, 2006, 2009). Annual hospital ECMO volume was analyzed as a continuous variable, with subsequent segregation into terciles (< 15 cases/yr. [low volume]; 15-30 cases/yr. [medium volume]; > 30 cases/yr. [high volume]). ECMO cases were segregated in respiratory or cardiac based upon indication. Cardiac cases were mapped to Risk Adjustment for Congenital Heart Surgery (RACHS) categories. Sampling weights provided by the KID were used to calculate national estimates. Weighted multivariable logistic regression was used to identify risk-factors for in-hospital mortality.

Results: Overall, 3867 cases were identified, yielding a national estimate of 6329 ± 495 cases. Of these, 591 ± 97 (12%) were respiratory runs, and 5738 ± 487 (88%) were cardiac runs. Overall cardiac ECMO cases increased significantly over time, from 553 ± 90 cases in 2000 to 2138 ± 218 cases in 2009. Cardiac ECMO cases had significantly higher in-hospital mortality (2660 ± 223 ; 46%) compared to respiratory ECMO cases (230 ± 43 ; 39%), $P=0.03$. Annual ECMO volume tercile was significantly associated with reduced in-hospital mortality ($P=0.01$) within nearly all RACHS categories (**Figure**). After adjustment for RACHS category and other patient variables lower ECMO volume group remained an important determinant of in-hospital death (Odds ratio 1.75; 95% Confidence Intervals: [1.03 - 2.94], $P=0.03$).

Conclusions: Higher ECMO case volume is associated with improved hospital survival in pediatric ECMO patients regardless of indication. For cardiac ECMO, annual ECMO case volume is an independent predictor of ECMO survival even when comparing patients of similar clinical complexity. Although ECMO survival is dependent upon many factors, the results of this study support the paradigm of regionalized centers of excellence for managing pediatric ECMO patients.

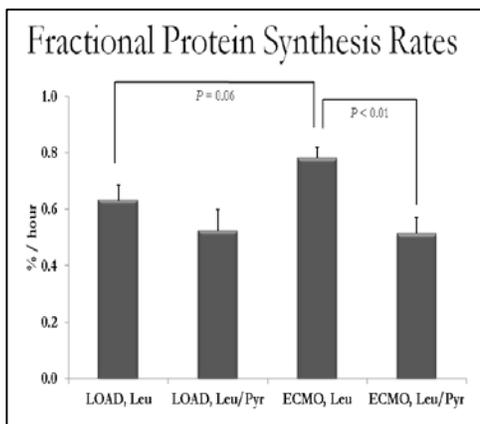


EXTRACORPOREAL MEMBRANE OXYGENATION PRESERVES MYOCARDIAL PROTEIN SYNTHESIS WITHOUT ALTERING LEUCINE OXIDATION IN IMMATURE SWINE IN VIVO

O'Kelly Priddy C, Kajimoto M, Ledee D, Bouchard B, Isern N, Olson A, Des Rosiers C, Portman M

Background: Mechanical unloading of the heart by ECMO induces changes for myocardial substrate metabolism and signaling for protein synthesis and degradation, though these signaling changes do not necessarily correlate with actual changes in protein synthesis. We hypothesized that mechanical unloading of the heart modifies the rate of protein synthesis in coordination with the relative leucine oxidative contribution via acetyl-CoA, and tested this in our established model using immature swine and cardiopulmonary bypass.

Methods: 20 male piglets (27-41 days of age, 7.8-14.5 kg) were separated into four groups based on loading status (normal circulation: LOAD, cardiopulmonary bypass: ECMO) and substrate provision into the LAD coronary artery ($[^{13}\text{C}_6, ^{15}\text{N}]$ -L-leucine alone or with $[2\text{-}^{13}\text{C}]$ -pyruvate) and maintained under general anesthesia for eight hours. The LAD infusion was given over the last hour of the protocol, and the heart was rapidly excised and frozen for metabolic analysis. Heart tissues then underwent ^{13}C isotopomer analysis by both GCMS and MRS to evaluate the leucine contribution to metabolic pathways via acetyl-CoA. Western blots were performed to evaluate signaling for protein synthesis.



Results: MRS analysis revealed that unloading maintains, while pyruvate inhibits, oxidation of leucine. GCMS analysis demonstrated significant reduction of intracellular free leucine enrichment by both unloading and pyruvate. Total citric acid cycle intermediate enrichment was significantly increased in the presence of pyruvate; no significant difference was identified by loading status alone. Fractional protein synthesis rates were calculated and indicated a trend toward increased protein synthesis with ECMO in the group that received leucine alone. The inclusion of pyruvate with ECMO significantly decreased the rate of protein synthesis. Western blotting confirmed significantly increased signaling for protein synthesis via increased phosphorylation of mTOR and decreased phosphorylation of eukaryotic elongation factor-2 (eEF-2) in ECMO subjects.

Conclusions: Leucine participates in and provides integration between two major biological pathways in heart: conversion to acetyl-CoA with entry into the citric acid cycle and incorporation as an amino acid building block into protein. Leucine oxidation is inhibited by supplying other sources for acetyl-CoA, such as pyruvate. However, ventricular unloading (ECMO) maintains leucine oxidation and relative contribution to the citric acid cycle. ECMO also maintains or marginally increases protein synthesis, as determined by leucine incorporation. Signaling for increased protein synthesis appears to occur through the mTOR pathway. Our results challenge prior theories proposing that decreased protein synthesis plays an important role in atrophic remodeling during ventricular unloading. Furthermore, we show that substrate manipulation can alter protein synthesis in the heart.

TOLL-LIKE RECEPTOR 4 MEDIATED LUNG ISCHEMIA-REPERFUSION INJURY: SIGNALING BEYOND MYD88 AND TIRAP

Phelan P, Merry H, Mulligan M

Introduction: The alveolar macrophage initiates a complex cascade of inflammatory stimulation in response to ischemia and reperfusion in the lung. Work in our laboratory has demonstrated TLR-4 as the critical receptor of the alveolar macrophage responsible for IR injury development. TLR-4 signals via two distinct pathways; the MyD88-TIRAP pathway and the TRAM dependent pathway. To further understand the TLR-4 signaling events required for the initiation of lung IR injury, we examined the role of these independent pathways by manipulating their proximal adapter proteins in both an in vivo hilar occlusion rat model and an alveolar macrophage primary cell culture model of hypoxia and reoxygenation.

Methods: Male Long-Evans rats were treated with vehicle or 20nmol of siRNA directed against TIRAP, MyD88 or TRAM prior to undergoing the ischemia-reperfusion protocol. During this procedure rats from each treatment group underwent either a left thoracotomy alone or thoracotomy plus temporary left hilar clamping for 90 minutes, followed reperfusion and re-ventilation.

Pulmonary capillary permeability was measured by lung tissue BSA-I-125 accumulation at 4 hours of reperfusion. MAPK phosphorylation was assessed by western blot after 15 minutes of reperfusion.

Primary cultures of alveolar macrophages were harvested from male Long-Evans rats. The cells were then treated with saline, non-coding siRNA, or siRNA for TLR-4, TRAM, MyD88 or TIRAP. After 2 treatment doses cells either remained at normoxia or underwent 2 hours of hypoxia and reoxygenation for up to 4 hours. Cell culture media was then harvested and proinflammatory cytokine production was measured with ELISAs for TNF- α and IL-1 β . Total protein from the cells was also harvested and examined for SAPK activation and protein knockdown.

Results: Injection of TIRAP, TRAM and MyD88 siRNA decreased target protein levels in alveolar macrophages by >95% when compared to animals injected with vehicle only. Knockdown of MyD88 or TIRAP resulted in significantly reduced PIs compared to vehicle treated positive controls: 68% and 36% reductions, respectively. Knockdown of TRAM resulted in PIs equivalent to controls.

Efficacy of in vitro siRNA uptake was confirmed by IHC with biotinylated siRNA. Target protein knockdown was confirmed with western blot analysis of targeted protein level. With TLR-4 knockdown, the secretory response and SAPK activation was equivalent to normoxic controls. MyD88 or TIRAP knockdown there was significant protection from injury, but to a lesser degree than TLR-4 knockdown. TRAM knockdown provided no protection, and the markers of injury were equivalent to reoxygenated controls.

Conclusion: TLR-4 is functionally required for lung ischemia reperfusion injury development. Injury primarily occurs through the MyD88-TIRAP dependent pathway. While both MyD88 and TIRAP are required for full injury development, some inflammatory signaling persists with each alone. TRAM dependent signaling is not independently involved in reoxygenation injury development in the alveolar macrophage.

LUNG CANCER MORTALITY AND RESIDENTIAL SEGREGATION IN THE UNITED STATES

Hayanga A, Zeliadt S, Backhus L

Introduction: Lung cancer mortality rates vary with race and geographical location. We sought to examine this relationship and the effect of residential segregation.

Methods: We examined age-adjusted lung cancer mortality rates from 2003-2007 in each county in the US for blacks and for the overall population. Our primary independent variable was the racial index of dissimilarity. The index is a demographic measure which assesses the evenness with which whites and blacks are distributed across census tracts within each county. The score ranges between 0 and 100. A value of 0 indicates whites and blacks are evenly distributed across and higher values indicate increasing degrees of residential segregation. Data was obtained from the 2009 Area Resource File (ARF), the National Center for Health Statistics, and the County Health Rankings project from the Wisconsin Population Health Institute and Robert Wood Johnson Foundations. A generalized linear model with a Poisson distribution and log link was used to examine the association between residential segregation and lung cancer mortality, with adjustment for population density, smoking rates, obesity rates, county income levels, and availability of oncology services.

Results: Each additional level of segregation was associated with a 0.3% increase in lung cancer mortality for blacks ($p=0.007$), with no associated increase in mortality for the overall population ($p=0.305$). Adjusted lung cancer mortality rates among blacks were 53.7 (s.d 1.9), 56.7 (s.d. 2.3), and 60.6 (s.d. 2.8) per 100,000 in counties with little segregation (<25% segregation), moderate segregation (25-50%) and high segregation (>50%) respectively. In contrast, the adjusted lung cancer mortality rates for the overall population were lower than rates among blacks, and were similar across counties regardless of the level of segregation 51.0 (s.d 0.09), 50.7 (s.d 0.11), and 50.4 (s.d 0.12) per 100,000, across the respective levels of segregation among US counties.

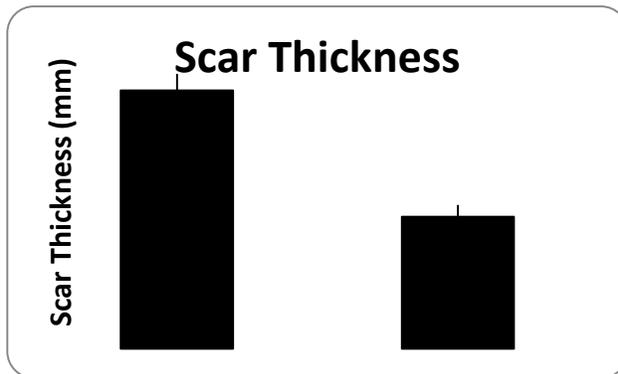
Conclusion: Lung cancer mortality is higher in blacks compared to whites in the US. Furthermore, it is highest in blacks living in the most segregated counties. Understanding the impact of racial segregation and its effect on lung cancer outcomes will further guide the implementation of measures to address healthcare disparities in the US.

EFFECT OF TOPICAL MAPK INHIBITION ON HYPERTROPHIC SCARRING IN A DUROC PORCINE MODEL

Chung C, Warsen A, Hocking A, Numhom S, Engrav L, Arbabi S

Background: Burns are one of the leading causes of morbidity and mortality in the United States. Inflammatory signaling pathways, such as p38 mitogen activated protein kinase (MAPK) play an important role in a patient's response to injury. We have previously shown that the application of topical p38 MAPK inhibitor on burn wounds attenuates inflammatory signaling and improves outcomes in a murine burn model. However, to study the effect of topical p38 MAPK inhibition on wound healing, a model that resembles the human response is required. The red Duroc porcine model has been an established animal model that closely mimics humans with respect to wound healing and hypertrophic scarring. In this study, we evaluate the efficacy of topical p38 MAPK inhibition on wound healing and scarring in the red Duroc pig model. Since p38 MAPK hyperactivation is associated with hyper-inflammatory response and hypertrophic scarring, we hypothesized that topical p38 MAPK inhibition will improve wound healing and decrease scar formation.

Methods: Eight week old red Duroc pigs received 10 tangential deep partial thickness wounds (5x5 cm) on their backs using a standard electric Padgett dermatome. Topical p38 MAPK inhibitor was applied over the wounds. Biopsies were taken at 2 weeks and 5 months. Periodic wound assessments with photographs were taken. Histological analysis was performed. The results were compared to red Duroc pigs that had no treatment in our previous experiments.



Results: There was an excellent re-epithelialization and wound closure in the treatment groups. Application of topical p38 MAPK inhibitor reduced the scar thickness, a measure of hypertrophic scarring, 5 months post-wounding ($p < 0.000009$) (Figure).

Conclusions: This pilot study showed that topical p38 MAPK inhibition did not interfere with re-epithelialization and wound closure. Inhibition of p38 MAPK resulted in reduced scar thickness

which suggests a potential in reducing hypertrophic scarring. Further experiments are required to explore other parameters of hypertrophic scarring, e.g. wound contraction, as well as to investigate the attenuation in inflammatory response. Application of topical p38 MAPK inhibitors to patients suffering from burn injuries may not only reduce their mortality and end-organ dysfunction, but also improve their cosmetic and functional outcome.

TRANSPLANTATION OF VASCULARIZED COMPOSITE ALLOGRAFTS IN A MISMATCHED SETTING WITHOUT THE NEED FOR CHRONIC IMMUNOSUPPRESSION

Chang J, Butts T, Graves S, Storb R, Mathes D

Background: Reconstruction for complex defects of hand or face requires the use of flaps, skin grafts, and prostheses. Although adequate, problems with form, function, and donor site morbidity are seen. Another strategy to approach these difficult reconstructions is transplantation of a cadaveric graft consisting of the same tissues, referred to as vascularized composite allografts (VCA). A major hurdle towards widespread adoption of VCA transplantation is due to its requirement for chronic immunosuppression and the associated complications with such agents. Furthermore, all hand and face recipients experience episodes of acute rejection despite being on immunosuppression.

From our previous studies, we were able to successfully demonstrate immunological tolerance towards VCA transplants in a matched large animal model using a mixed chimera protocol. Here, the purpose of this experiment was to extend these transplants in a mismatched setting. Tolerance towards mismatched VCA would prevent episodes of acute rejection and eliminate the need for chronic immunosuppression.

Hypothesis: Immunological tolerance towards mismatched VCA can be induced by simultaneously transplanting donor stem cells and donor VCA into the recipient.

Design: Eight dog transplants were performed across a single haplotype DLA mismatched barrier. All dogs received 450 cGy of radiation on the day of transplant. They then underwent a VCA transplant (Myocutaneous rectus flap) with four dogs receiving donor peripheral mobilized stem cells and four dogs receiving donor bone marrow. All recipients received post-grafting immunosuppression (35 days of Cyclosporine and 28 days of Mycophenolate Mofetil). They were followed for donor cell chimerism in their peripheral blood. The allografts underwent routine biopsies and were followed clinically.

Results: Of the four dogs receiving donor mobilized stem cells, all four demonstrate tolerance towards their mismatched VCA transplants. However two of the four dogs developed full donor chimerism and ultimately GVHD. Of the two dogs not developing GVHD, one dog completely lost donor chimerism by 20 weeks post-transplant yet continued to be tolerant of the donor VCA.

Of the four dogs receiving donor bone marrow, only one dog demonstrated tolerance towards the VCA whereas the other three dogs rejected their VCA, coinciding with rejection of donor marrow. In the tolerant dog, there is full donor chimerism.

Conclusion: This study demonstrates that in a mismatched setting, simultaneous transplant of donor mobilized stem cells and VCA leads to tolerance towards both the skin and muscle of the transplant. The use of donor bone marrow as a source of cells is insufficient to reliably induce tolerance across a mismatched barrier with our current induction protocol. Tolerance induction appears to be dependent on the administration of stem cells but maintenance of tolerance towards VCA may not require the persistence of donor cell chimerism.

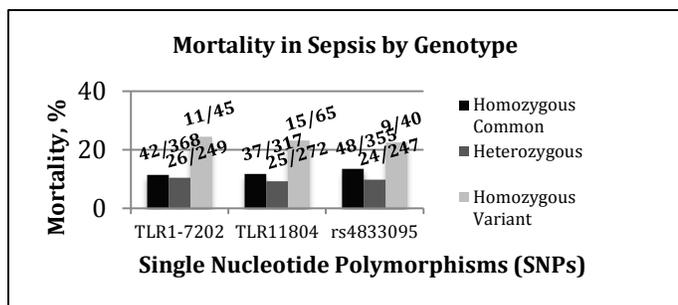
TOLL-LIKE 1 RECEPTOR POLYMORPHISMS AND ASSOCIATIONS WITH OUTCOMES IN SEPSIS FOLLOWING TRAUMATIC INJURY

Thompson C, Wurfel M, O'Keefe G

Background: Genetic variation (single nucleotide polymorphisms [SNPs]) has been associated with both the risk for and outcome from infection in critically ill patients. Most findings have not been replicated, calling into question the originally reported association. Two SNPs in the toll-like receptor 1 (TLR1) gene (TLR1-7202A/G and TLR1_{1804G/T}) have previously been shown to predispose to a higher inflammatory response *ex vivo* and have been associated with higher mortality and organ dysfunction in sepsis as well as a higher prevalence of gram-positive sepsis in a primarily medical intensive care unit (ICU) cohort.

Purpose: To determine whether TLR1 variation (TLR1-7202A/G and TLR1_{1804G/T}) is associated with mortality after traumatic injury.

Methods: Severely injured patients admitted to the ICU at Harborview Medical Center were enrolled with IRB approval. Demographic and clinical data were collected from the electronic medical record and the trauma registry. The primary outcome measured was mortality. Patient samples were genotyped for TLR1-7202A/G and TLR1_{1804G/T} and a 3rd, nonsynonymous SNP (rs4833095_{A/G}) that is in significant linkage disequilibrium with TLR1-7202A/G. Genotypes were determined by TaqMan-based real-time polymerase chain reaction (RT-PCR) or Restriction Fragment Length Polymorphism (RFLP) Probes. Statistical analysis was completed using Stata 12. Categorical data were compared by χ^2 analysis and continuous data were analyzed using Student's t-test. Logistic regression analysis adjusted for age, injury severity score, head abbreviated injury scale score and sex was used to determine odds ratios. We assumed a recessive effect of the allele on the phenotype. To minimize the risk of confounding due to racial differences in SNP frequency, we limited our analysis to Caucasian patients.



Results: A total of 1,498 Caucasian patients were successfully genotyped. Of those patients 1,426 were genotyped for TLR1-7202A/G, 1,406 for TLR1_{1804G/T}, and 1,394 for rs4833095_{A/G}. We confirmed associations between mortality in sepsis and both TLR1-7202G (OR, 3.13; $P=0.004$) and TLR1_{1804T} (OR, 2.48; $P=0.008$). More specifically, we found an association between mortality in gram-positive sepsis and TLR1-7202G (OR, 4.05; $P=0.021$). Additionally, the nonsynonymous SNP (rs4833095_G) was associated with mortality in patients with sepsis (OR 2.42; $P=0.038$) and particularly in patients with gram-positive sepsis (OR 3.79; $P=0.028$). TLR1 variation was not associated with mortality in the absence of gram-positive infection.

Discussion: We have identified an association between TLR1 genetic variation and mortality after severe traumatic injury. Our findings confirm the results of a previous report and extend those observations by identifying an association with a nonsynonymous SNP that changes the TLR1 amino acid sequence. Our observation suggests that genetic differences that affect TLR1 structure determine clinical outcomes in gram-positive infection after severe trauma.

Alveolar Dead Space Correlates with Early Mortality in Trauma Patients

Garland T, Warner K, Bulger E, Evans H, Jurkovich G, Cuschieri J

Background: Early identification of trauma patients requiring urgent lifesaving intervention is problematic. Predictors such as hypotension, tachycardia and level of consciousness are overall poor predictors of early death and hemorrhagic shock. The arterial and end-tidal carbon dioxide (Pa-EtCO₂) derived alveolar dead space (VD_{alv}) is representative of pulmonary perfusion, and thus cardiac output. We hypothesize that VD_{alv} will represent an easily obtainable perfusion deficit that correlates with outcome.

Methods: Patients were included if they were intubated and had EtCO₂ values recorded in the Emergency Department. Patient demographics and injury characteristics were obtained. Presenting heart rate (HR), SBP, EtCO₂, ABG, base deficit and lactate were recorded and receiver operating characteristics (ROC) and univariate logistic regression were used to evaluate requirement of emergent blood transfusion and mortality rates.

Results: Area under the ROC curve demonstrates prediction of early death by VD_{alv} (AUC=.796), base deficit (AUC=0.665), lactate (AUC=0.661), and first blood pressure (AUC=0.681). Logistic regression demonstrates correlation of death with predictors using commonly used clinical cutoffs VD_{alv} >0.3 (OR=8.61, 95%CI 3.0-225), base deficit >6 mEq/L (OR=2.6, 95%CI 0.97-7.1), blood pressure <90mmHg (OR=2.1, 95%CI 0.71-6.0) and lactate >4mmol/L (OR=2.1, 95%CI 0.95-5.8).

Conclusion: Patients at risk of early death after trauma are difficult to diagnose accurately in the absence of uncompensated shock. Pa-EtCO₂ derived VD_{alv} is an easily calculable variable that predicts the patients at risk for early mortality better than current measures.

COMPLIANCE WITH CDC FIELD TRIAGE GUIDELINES IN AN ESTABLISHED TRAUMA SYSTEM

Gage A, Traven N, Rivara F, Cuschieri J, Jurkovich G, Arbabi S

Background: Trauma systems provide optimal care in an organized approach to acutely injured patients. Regionalization of trauma care reduces mortality and has clear guidelines for transport to highest level of trauma care. In 2006, the CDC updated its Field Triage Decision Scheme. The decision scheme has four criteria – physiologic, anatomic, mechanism, and special considerations. Whether prehospital providers are following CDC triage decision points in an established trauma system remains to be determined.

Purpose: To determine what prehospital patient characteristics dictate which trauma patients are transported directly to a Level I trauma center and to determine if prehospital providers are following CDC guidelines for the triage of injured patients in an established trauma system.

Methods: Retrospective cohort analysis of 5 years (2004-2008) of collected data in Washington State’s Central Region Trauma Registry (CRTR) and King County Emergency Medical Services (KCEMS) database based on geocode mapping. Patients were analyzed based on transportation to their designated hospital or direct scene transport to the Level I center.

	Stayed at Level III-V	Transferred to Level I	Direct to Level I
N of cases	5024	1106	3240
% female	53.5%	34.3%	27.8%
Age	57.3	44.4	36.5
Scene GCS	14.6	14.4	13.1
Scene SBP	137.4	135.0	128.7
ISS	7.4	12.8	17.0
<i>Discharge status</i>			
% to home	46.3%	67.2%	70.0%
% to homecare	9.8%	3.5%	3.7%
% to SNF	28.9%	15.0%	11.1%
% to rehab	3.0%	2.4%	6.5%
% died	1.8%	1.8%	6.9%

Results: A total of 12,106 patients were included in the study, of which 5,976 (49.4%) were transported directly to a Level I center, 5,024 (41.5%) transported to a Level III-V and 1,106 (9.1%) transported to a Level III-V first and then transferred to a Level I center. Patients transported directly to a Level I trauma center were more likely to be male, younger, have a penetrating injury, lower scene GCS, lower scene blood pressure, and be intubated at the scene. Level I direct scene transports were significantly less likely for older patients. Compared with patients ages 18 to 45, the adjusted odds ratio for direct transport to the Level I was 0.7 (95% CI 0.59-0.83) for ages 46-55, 0.47 (95% CI 0.39-0.57) for ages 56-65, 0.28 (95% CI 0.23-0.34) for ages 66-80, and 0.11 (95% CI 0.09-0.14) for ages \geq 81.

Conclusions: In an urban, organized trauma region, pre-hospital providers are following CDC triage guidelines on steps 1 through 3. However, contrary to step 4 recommendations, older age was associated with transport to lower levels of trauma care in our region.

MORTALITY ASSOCIATED WITH GRAM NEGATIVE BACTEREMIA MAY REFLECT EARLY ALTERATIONS IN INNATE IMMUNITY AFTER SEVERE TRAUMATIC INJURY

Park C, O'Keefe G

Background: Nosocomial bacteremia is a serious clinical complication that, in some studies, has been associated with increased mortality in critically ill patients.

Purpose: We sought to determine the association between bacteremia and outcomes after traumatic injury. We used genome-wide gene expression data, to identify early alterations in innate immunity, hypothesizing that these differences might lead to subsequent immune suppression and bacteremia.

Methods: Using the clinical data gathered by Inflammation and the Host Response to Injury (Glue Grant) project, the relationships between the bacteremia and the outcome following severe trauma were examined. All continuous data were compared using the Mann-Whitney-U test and categorical data using Pearson's Chi Square. This was followed by step-wise logistic regression to determine the association between bacteremia and death, adjusting for other important factors.

Where available, total peripheral leukocyte RNA, was analyzed, looking for differences in genome-wide gene expression between patients who progressed to bacteremia and those who did not. We used Ingenuity Pathway Analysis and GeneGo Metacore 6.6 to assess these differentially expressed genes for ontology and function.

Results: A total of 252 patients developed bacteremia. Patients with bacteremia had a higher risk of death (RR = 1.5, 95% CI 1.1-2.1) and prolonged ICU stays (21 days vs. 9 days). After adjusting for important mortality risk factors (age, APACHE II score, amount of blood transfused), gram negative bacteremia, but not gram positive bacteremia, was associated with an increased mortality risk (OR = 1.8). We then focused on determining whether patients who developed gram negative bacteremia had early gene expression profiles that differed from patients who did not develop gram negative bacteremia. We found 132 genes on day 1 and 32 genes on day 4 that predict susceptibility to gram negative infection with 100% sensitivity and 99% specificity at both time points. Overall, the genes that were differentially expressed were in inflammatory response pathways. For example, on day 1, suppression of MHC class I genes was evident in the patients who developed gram negative bacteremia. By day four, additional immune-related genes were expressed at lower levels in patients who developed gram negative bacteremia.

Conclusions: Gram negative bacteremia is associated with a nearly 2-fold increase in mortality after traumatic injury. Patients who develop gram negative bacteremia have early changes in leukocyte gene expression that are consistent with suppression of innate immunity.

INTRAVASCULAR ULTRASOUND: A CRITICAL TOOL FOR ACCURATE ENDOGRAFT SIZING IN BLUNT TRAUMATIC AORTIC INJURY

Wallace G, Hatsukami T, Quiroga E, Starnes B, Tran N

Background: Aortic diameter is dynamic with respect to a patient's volume status. This may lead to under-sizing of an endograft in the endovascular repair of blunt traumatic aortic injury (BTAI) if imaging used for planning is obtained when the patient is hypovolemic. We aim to quantify changes in thoracic aortic diameter as measured by initial computed tomographic angiography (CTA) compared to intravascular ultrasound (IVUS) at the time of endovascular repair and/or post-implant CTA in trauma patients with BTAI.

Methods: We retrospectively evaluated all trauma patients with BTAI admitted to our level 1 trauma center from July 2007 to July 2011 who underwent initial admission or pre-admission CTA along with IVUS at the time of repair and/or post-implant CTA. CTA and IVUS images were reviewed at the level of the left subclavian artery. Differences in aortic diameter among the imaging groups were compared using the paired Student t-test. Graft sizes for theoretical repair of each of the measured aortic diameters were determined and compared among the imaging groups using the paired Student t-test.

Results: 16 patients with BAI were identified with initial CTA, IVUS, and post-implant CTA. Mean age was 39 ± 16.1 years (range 17-73) with 75% males, 69% transfers from outside hospitals, and mean ISS 41 (range 26-54). Mean time from initial CTA to IVUS was 28 hours (range 2h-5.5days) and from IVUS to post-implant CTA was 21 days (range 16h-55d). Mean aortic diameter was significantly larger when measured with IVUS vs initial CTA (+2.38 mm, $p=0.004$) and similarly significantly larger when measured on post-implant CTA vs initial CTA (+3.13 mm, $p=0.0001$). Mean aortic diameter on post-implant CTA vs IVUS was +0.75mm ($p=0.003$). Theoretical graft sizes based on IVUS and post-implant CTA were similar (0.6mm, $p=0.5$) and significantly larger when compared to theoretical graft sizes based on initial CTA (+2.4 and +2.9mm, $p=0.003$ and 0.0001 , respectively). An additional 6 patients were identified with only initial CTA and post-implant CTA, without IVUS. In this group, mean aortic diameter as measured on post-implant CTA was significantly larger compared to initial CTA measurements (+3.75mm, $p=0.002$).

Conclusion: The aortic diameter of patients with BTAI is significantly smaller when measured on the initial CTA vs IVUS at the time of repair and post-implant CTA measurements. This difference in aortic diameter may reflect hypovolemia and under-resuscitation in the critically ill trauma patient and can translate to an undersized endograft used in the endovascular repair of the patient with BTAI. The difference is smaller when measurements by IVUS are compared to post-implant CTA. Theoretical graft sizes for the aortic diameters measured with IVUS and post-implant CTA were the same, and both were significantly larger than theoretical endograft sizes based on the initial CTA. We endorse the routine use of IVUS as a critical tool for the real-time determination of the actual, resuscitated aortic diameter and subsequent sizing decisions at the time of repair of BTAI.

IMPACT OF GRADUATED COMPRESSIVE STOCKINGS ON THE PREVENTION OF POST THROMBOTIC SYNDROME: RESULTS OF A RANDOMIZED TRIAL

Jayaraj A, Meissner M

Background: Post-thrombotic syndrome (PTS) is a common chronic complication of acute deep venous thrombosis (DVT) in the lower extremity, with as many as two-thirds of patients developing symptoms of pain, edema, hyperpigmentation, or ulceration. The role of graduated compressive stockings (30-40mm Hg knee length) in the prevention of PTS has been studied with the opinion being divided on the beneficial effects. We aim to answer this question with a randomized controlled study that used multiple scoring instruments to assess post thrombotic syndrome.

Methods: 69 consecutive patients with an acute DVT diagnosed by duplex ultrasonography were randomized to treatment with graduated compressive stockings (GCS) or no stockings to assess the impact of GCS on prevention of PTS. Venous Clinical Severity Score (VCSS) and PTS scoring put forth by Villalta et al (VPS), commonly used scoring systems, were used to appraise PTS at 3, 6, 12, 18 and 24 months following diagnosis of DVT. In both scoring systems, the individual either had PTS (mild to moderate or severe) or no PTS. Cumulative incidence was computed using Kaplan Meier analysis. Relative risk for development of PTS was assessed for age (<50yrs), obesity, varicose veins and ileo-femoral DVT.

Results: As measured by both VPS and the VCSS instruments, the GCS group had a lower incidence of PTS (5% decrease per VPS and 10% decrease per VCSS) compared to the control group but only when 1 month was used as cut off time for first diagnosis of PTS. When 6 or 12 months was used there was no difference between the two groups in the incidence of PTS. Additionally, the burden of post thrombotic syndrome was significantly more when the VPS instrument (~75%) was used as compared to the VCSS instrument (~30%) at 24 months follow up. While Age (<50yrs), obesity, Ileo-femoral DVT and Varicose veins subgroups have increased incidence of PTS, only Obesity appears to be a statistically significant predictor.

Conclusion: As assessed by both VPS and VCSS instruments, the use of graduated compressive stockings does not appear to reduce the incidence of PTS. There appears to be a significant difference in the incidence of PTS as detected by VPS and VCSS instruments with incidence of PTS being dependent on the instrument and cut off time interval used to assess PTS.

PATIENT-LEVEL FACTORS ASSOCIATED WITH ANTIREFLUX PROCEDURES IN CHILDREN HOSPITALIZED WITH GASTROESOPHAGEAL REFLUX DISEASE

McAteer J, Garrison M, Larison C, Goldin A

Introduction: Gastroesophageal reflux disease (GERD) is one of the most common diagnoses in pediatric practices. Several studies have shown that there is significant variation among both providers and hospitals regarding treatment of GERD in children, and specifically regarding the use of antireflux procedures (ARP). Currently no data exist that identify associations across symptoms and comorbidities and the likelihood of undergoing ARP. Our aim was to identify objective patient-level factors associated with progression to ARP in pediatric patients hospitalized with GERD.

Methods: We conducted a case-control study of inpatients in the Pediatric Health Information System (PHIS) database. We identified all patients in the database younger than 19 years old discharged between 1 January 2002 and 31 December 2010 with primary diagnostic codes for GERD. The main outcome measure was the hazard ratio of progressing to an ARP, given the presence of multiple independent patient-level variables, including demographic factors and medical and surgical comorbidities.

Results: We identified 141,190 patients with a GERD hospitalization meeting study criteria. 11,621 (8.2%) patients underwent an ARP at some point during the study period. The proportional hazard of receiving an ARP was increased significantly in children with failure to thrive, neurodevelopmental delay, chromosomal anomalies, cardiopulmonary anomalies, cerebral palsy, aspiration pneumonia and those with certain surgical conditions (diaphragmatic hernia, hiatal hernia, malrotation, TE fistula). Each additional GERD-related hospitalization was associated with an incrementally increased hazard of receiving an ARP.

Conclusions: This study explores characteristics of a national cohort of pediatric patients hospitalized with a diagnosis of GER, and defines patient-level characteristics that are associated with an increased risk of progression to ARP. These results raise interesting questions regarding GERD treatment variability and the application of ARP to patient populations shown to respond less favorably to such procedures, such as patients with developmental delay and those with TE fistula. The findings in this study help to identify objectively variables that should be incorporated into future studies designed to decrease the variability in the evaluation, management, and outcomes of patients with GERD.

Cost-Effective Microsimulation Model of Negative Pressure Wound Therapy versus Standard Dressing in Acute Post-Surgical Wounds

Prucz R, Perkins J

Background: Compared to standard moisture dressings (SMD) negative pressure wound therapy (VAC) is thought to accelerate the healing and reduce the number of dressing changes in the management of chronic wounds at a lower cost. This therapy has been increasingly applied to acute surgical wounds, but data regarding its cost-effectiveness is limited. The purpose of this study is to determine if VAC is economically justifiable when compared to SMD in acute post-surgical wounds.

Methods: A Markov microsimulation cost-effective model was created to follow the surgical course from the time of opening an acute surgical wound until the wound was healed. Cost data from 2011 were obtained from our hospital. Effectiveness, measured in terms of pain with dressing changes and healing rates were determined by consensus from a literature review. Individual patients move through the model according to wound size (average 33.3 cm range 10 to 60 cm). Ten thousand patients were in the model to reach stability.

Results: Patients treated with VAC healed in 26.6 ± 5.5 days vs 36.9 ± 8.1 days for SMD ($p < 0.01$). The average cost of the VAC was $\$3522.20 + 741.20$ and effectiveness was 93.4 ± 0.94 compared to the SMD with cost of $\$1297.15 \pm 613.17$ and effectiveness of 90.25 ± 1.44 . The incremental cost effective ratio (ICER) was $\$706.67$.

Conclusion: Patients treated with VAC healed in less time and with less discomfort compared to SWD, but at significantly increased costs. While VAC may have a cost benefit in chronic wounds, this finding was not confirmed in acute post-surgical wounds. Large scale randomized studies are needed with emphasis on hospital discharge rates, clinic utilization, healing rates and pain evaluations.

THE MEDIUM TERM OUTCOMES OF BARRETT'S ESOPHAGUS IN PATIENTS TREATED WITH LAPAROSCOPIC ANTI-REFLUX SURGERY

Loviscek M, Wassenaar W, Bushyhead D, Hinojosa M, Pellegrini C, Oelschlager B

Background: Barrett's esophagus (BE) is caused by chronic gastro-esophageal reflux disease (GERD), and is the main cause of esophageal adenocarcinoma. Laparoscopic anti-reflux surgery (LARS) is the only treatment that addresses the underlying cause: GERD. The purpose of this study is to determine how well LARS improves symptomatic manifestations of GERD, esophageal function, and whether it can change the natural history of the Barrett's epithelium.

Methods: We reviewed prospectively collected data and clinical records and attempted to contact all patients who had a LARS > 3 years ago. We administered our standard GERD questionnaire to evaluate long-term changes in post-operative symptoms. Follow-up data included endoscopy findings, histology, pH and manometric studies. Regression of BE was defined as either the disappearance of intestinal metaplasia and replacement with normal mucosa or transition from dysplasia to intestinal metaplasia without signs of dysplasia (without any other endoscopic therapy). Progression of disease was defined as development of High grade dysplasia (HGD) or esophageal adenocarcinoma (EAC).

Results: Eighty patients at a median follow-up of 8 years (3-16 years). Eighty-six per cent of patients reported improvement in heartburn and regurgitation with a mean overall satisfaction of 8 (0-10). Thirty-four (43%) patients underwent pre- and early post-operative dual probe pH and manometry studies at a mean of 8 months (2-12 months). The mean DeMeester score decreased from 79 preoperatively to 29 postoperatively with 80% of patients having a normal DeMeester score. Thirty-six (45%) patients underwent pre- and post-operative manometric studies at a mean of 8 (2-12 months). The mean LES pressure increased from 11 to 18 mmHg. Long-term histological regression of BE occurred in seventeen patients (21%), specifically 14/80 with BE regressed to normal and 3/80 with dysplasia lost all evidence of dysplasia. Of those 14 patients who regressed to normal, 13 had a short segment of Barrett's, 1 had long segment (> 3cm), of these 6 had a normal post-operative DeMeester score and 2 an abnormal score. Of those 3 patients who lost all evidence of dysplasia, 1 had a short segment of Barrett's and 2 had long segment, 2 had normal DeMeester score and 1 abnormal. Histological progression of BE occurred in ten patients (6/80). Of those, four had long segment Barrett's.

Conclusions: LARS is associated with excellent control of GERD and related symptoms and it normalizes acid exposure in the majority of patients. Histological regression occurred in one fifth of this unselected series of patients with Barrett's. Normalization of acid exposure and short segment Barrett's appear to promote disappearance of Barrett's after LARS.

THE ACGME CASELOGS: CHANGES OVER TWO DECADES

Drake F, Kwon S, Aarabi S, Huntington C, Gow K

Background: Surgical training is experiential, requiring sufficient exposure to provide experience and technical competency. One metric available to assess this exposure is the number and variety of cases performed during residency. The Accreditation Council for Graduate Medical Education (ACGME) maintains a database of operative caselogs for graduating surgical residents. By reviewing the database, changes in the resident's operative experience may be identified.

Methods: ACGME caselogs for general surgery residents were available for trainees who graduated in academic year (AY) 1989-90 through 2009-10. The first decade (AY1989-90 through 1998-99 = Period A) was compared to the more recent decade (AY1999-2000 through 2009-10 = Period B). Statistical differences were evaluated using Student's T-test with a value of $p < 0.05$ as significant.

Results: The average number of training programs decreased from 267 in Period A to 249 in Period B. However, the number of residents remained stable, leading to a slight rise in average number of graduates per program. Total case numbers and categories with the five largest mean changes are presented in Table 1.

Table 1

Category	Period A (Mean cases/resident)	Period B (Mean cases/resident)
Total Major Operations (TMO)	898.25	902.85
Colon	99.98	122.09*
Hernia	79.87	97.89*
Skin/Soft-tissue	16.65	34.48*
Biliary	91.91	109.71*
Endocrine	19.87	29.59*
Gynecology	9.08	3.24*
Pediatric	45.22	37.77*
Genitourinary	17.21	7.41*
Vascular access	69.25	45.34*
Trauma	63.47	38.74*

*Denotes significant statistical difference between Period A and Period B

Conclusions: Despite changes in numerous aspects of surgical training, comparison of two extended periods reveals that General Surgery residents have maintained overall case numbers. However, changes in case-mix have narrowed the spectrum of experience. Therefore today's surgical trainee will graduate with a different skill set than his or her predecessors, which may lead to a decline in surgeons capable of addressing with the broad array of surgical issues.

Outcomes of Nissen Fundoplication in Patients with Concurrent Idiopathic Pulmonary Fibrosis and Gastroesophageal Reflux

Hinojosa M, Figueredo E, Kwon Y, Pellegrini C, Raghu G, Oelschlager B

Introduction: Idiopathic Pulmonary Fibrosis (IPF) is a progressive type of interstitial lung disease characterized by a radiographic appearance of usual interstitial pneumonia accompanied by an irreversible decline in pulmonary function (10% per year). With a uniformly fatal outcome and a median life expectancy of 2-4 years from the date of diagnosis, IPF poses a frustrating challenge to clinicians. Recent work has shown that microaspiration of esophageal refluxate in the context of gastroesophageal reflux disease (GERD) in patients with IPF significantly contributes to their pulmonary decline. It has thus been postulated that steps taken to mitigate reflux may have a significant role in stabilizing the decline of patients with IPF. The purpose of this study was to demonstrate that Nissen funduplications can be performed safely, with low morbidity and no mortality in patients with concurrent IPF and GERD, as well as whether doing so might stabilize pulmonary function.

Methods: We reviewed charts of patients referred to the Center for Esophageal and Gastric Surgery at the University of Washington with IPF and concurrent GERD, who underwent a laparoscopic Nissen fundoplication. Outcome measures included 24-hour pH study, intraoperative complications, length of hospital stay, length of ICU stay, morbidity, mortality, and progression of IPF (by FVC and acute pulmonary events).

Results: Eight patients with a mean age of 64 +/- 9 years met our inclusion criteria and underwent Nissen fundoplication. Preoperatively mean distal percent time pH less than 4 was 7.8 +/- 5.7 and mean DeMeester score was 40 +/- 24. Postoperative mean distal percent time pH less than 4 decreased (1.15 +/- 1.3) as did the mean DeMeester score (13.4 +/- 17). There were no intraoperative complications. Mean length of hospital stay was 3.1 +/- 1.9 days with a mean ICU stay of 0.5 +/- 0.8 days and all patients were discharged to home. There were 2 complications (central venous line infection and severe gastric distention needing endoscopic intervention) and 1 readmission (central venous line infection). Mean preoperative percent expected forced vital capacity was 63.3% +/- 13.5% and postoperatively was 63.4% +/- 17.2% with a mean of 35 months post operatively.

Conclusions: Nissen fundoplication in patients with IPF can be performed safely with minimal morbidity and no mortality. Furthermore, laparoscopic antireflux surgery may limit the disease progression of IPF in the setting of GERD by eliminating microaspiration of esophageal refluxate.