Presentation #1 | Basic Science | General Surgery

THE EFFECT OF REDUCED O-GLCNAC TRANSFERASE ON THE SEVERITY OF ACUTE PANCREATITIS

Mackenzie M. Moore and Emilyn U. Alejandro

Presenter: Mackenzie Moore MD University of Minnesota

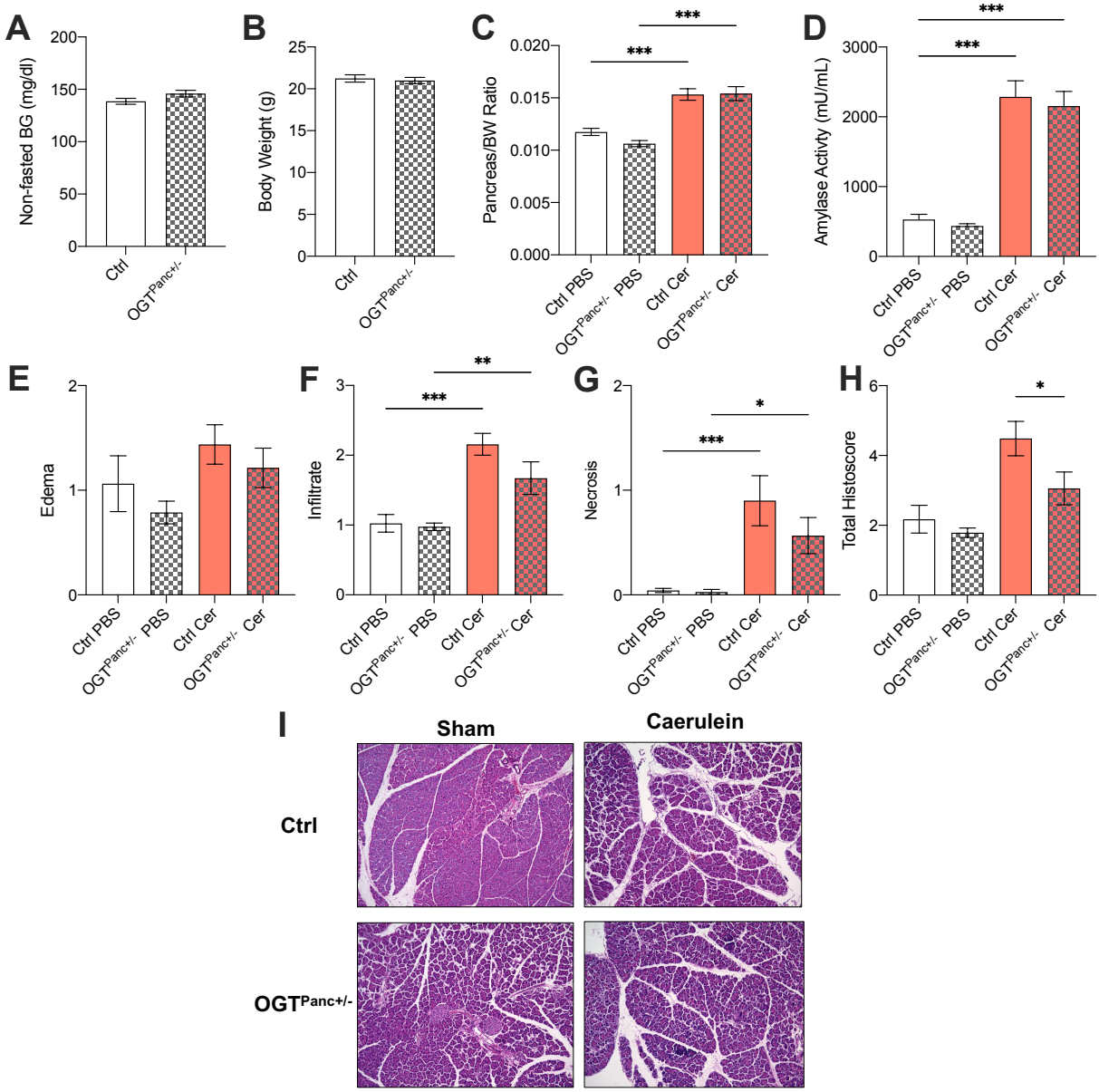
Background: Acute pancreatitis (AP) involves the premature activation of trypsin which leads to a cascade of pro-inflammatory signaling, NF-κB activation, and organelle dysfunction in the acinar cells which can lead to a severe systemic inflammatory response. O-GlcNAc transferase (OGT) is an enzyme that regulates multiple components of this cascade. The role of OGT has been studied in several inflammatory conditions where its effects appear to be specific to the physiological context. In vitro studies have demonstrated that reducing OGT decreases the severity of pancreatitis, but in vivo studies are lacking.

Objective: This study aims to determine if a pancreas-specific transgenic reduction of OGT in a mouse model affects the severity of AP. We hypothesize that a decrease in OGT will reduce the severity of AP.

Method: Mice with reduced pancreatic OGT (OGTPanc+/-) were generated utilizing the Cre-Lox system. At 8-10 weeks of age, mice were randomized to caerulein, which induces pancreatitis, or PBS injections. Theseverity of pancreatitis was scored based onhistology. Serum levels of IL-1β, IL-6, and TNF-α were obtained as well as amylase, lipase, and LDH. Trypsin and NF-κB activity were evaluated in pancreatic tissue.

Results: Mice with reduced pancreatic OGT had similar body weight and blood glucose to controls. This indicates that malnutrition or hyperglycemia are not likely contributing to differences between OGTPanc+/- mice and controls. AP was confirmed by elevated amylase levels and on histological analysis. The histological scoring demonstrated that OGTPanc+/- mice had a decreased severity of AP compared to controls (p=.02).

Conclusion: In this mouse model, a reduction of pancreatic OGT attenuates the severity of acute pancreatitis which is consistent with previous in vitro studies. Future studies are needed to explore the inhibition of OGT as a potential therapeutic approach.


A
Non-fasted BG (mg/dl)
200
150
100
50
0
Ctrl
OGTPanc+/-
B
Body Weight (g)
25
20
15
10
5
0
Ctrl
OGTPanc+/-
C
Pancreas/BW Ratio
0.020
0.015
0.010
0.005
0.000
***
***
Ctrl PBS
OGTPanc+/- PBS
Ctrl Cer
OGTPanc+/- Cer
D
Amylase Activty (mU/mL)
3000
2000
1000
0
***
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Ctrl PBS
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Sham
Caerulein
Ctrl
OGTPanc+/-

Presentation #2 | Basic Science | Bariatric Surgery

LAPAROSCOPIC VERTICAL SLEEVE GASTRECTOMY IN NONHUMAN PRIMATES MODULATES VISCERAL ADIPOSE TISSUE INFLAMMATION WITH A DECREASE IN CD40-EXPRESSING CELLS

Julia L. Nugent, Meghan Moore, Laura Hocum Stone, Amar Singh, Sabarinathran Ramachandran, Sayeed Ikramuddin, Melanie L. Graham

Presenter: Julia Nugent MD University of Minnesota

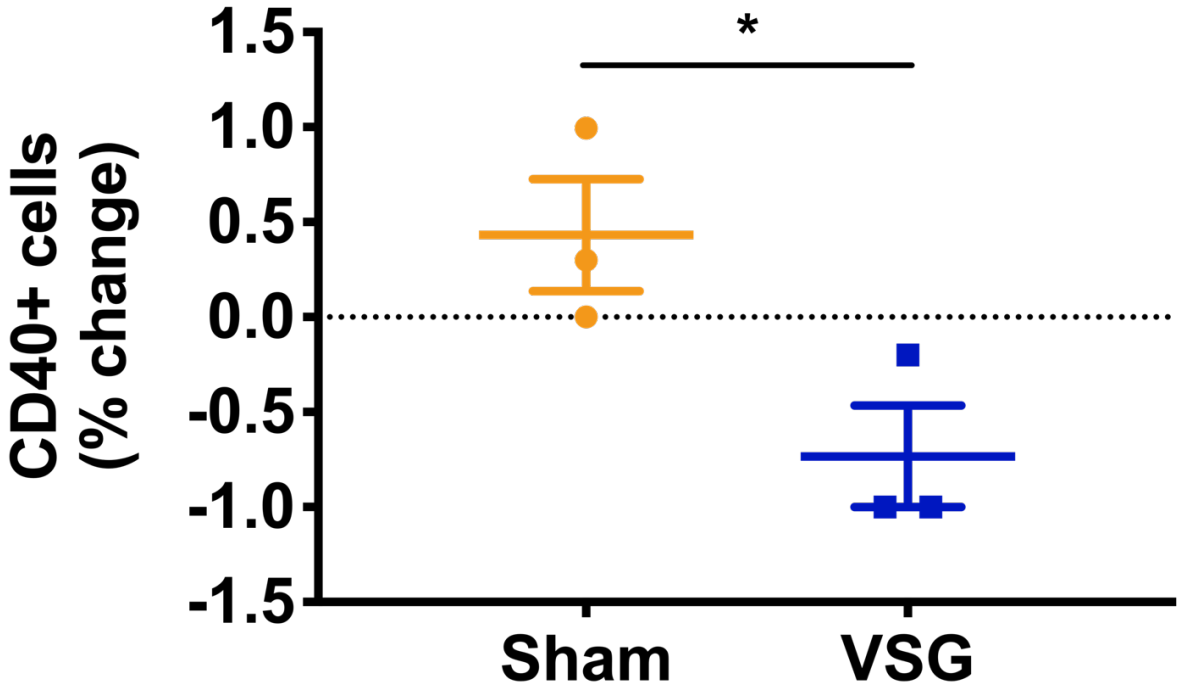
Background: Obesity is a disease of low-grade inflammation of the visceral adipose tissue (VAT), which is associated with development of metabolic disease and related comorbidities. The costimulatory receptor CD40 is expressed by antigen-presenting cells and induces inflammation once bound by sCD40L on T cells, and is likely a critical player in VAT inflammation. Bariatric surgery is the most effective treatment for metabolic disease and reduces VAT inflammation, yet its effect on CD40 expression is not described.

Objective: We sought to evaluate CD40 expression in the VAT after vertical sleeve gastrectomy (VSG) in a preclinical nonhuman primate model.

Method: Six spontaneously obese macaques underwent laparoscopic VSG or sham surgery (division of the omentum/short gastrics without sleeve creation). CD40 immunohistochemistry was performed on VAT from the day of surgery and 1 year postoperatively using a Dako Autostainer. A multiplex cytokine assay was used for peripheral serum analysis.

Results: One year after VSG, CD40-expressing cells in the VAT were significantly reduced compared to sham surgery (percent change from preoperative values: -0.73±0.27 versus 0.43±0.29, $p=0.04$). Peripheral serum sCD40L was not significantly different between VSG or sham surgery.

Conclusion: In this translational model, we observed a significant reduction in CD40+ cells in the VAT following VSG indicating a reduction in VAT inflammation resulting in improved systemic insulin sensitivity. These findings enhance our understanding of the role of CD40 signaling in chronic VAT inflammation and suggest co-stimulation blockade as a possible therapeutic target to improve the success and durability of bariatric surgery for patients with metabolic syndrome.


CD40+ cells
(% change)
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
*
Sham
VSG

Presentation #3 | Clinical Science | General Surgery

SKIN GRAFT PLACEMENT AROUND FISTULAS AND OSTOMIES WITH OPEN WOUNDS: A NOVEL SURGICAL TECHNIQUE

Bobel, MC; Obst, M; Miotke, S; Schlaefer J

Presenter: Matthew Bobel MD University of Minnesota

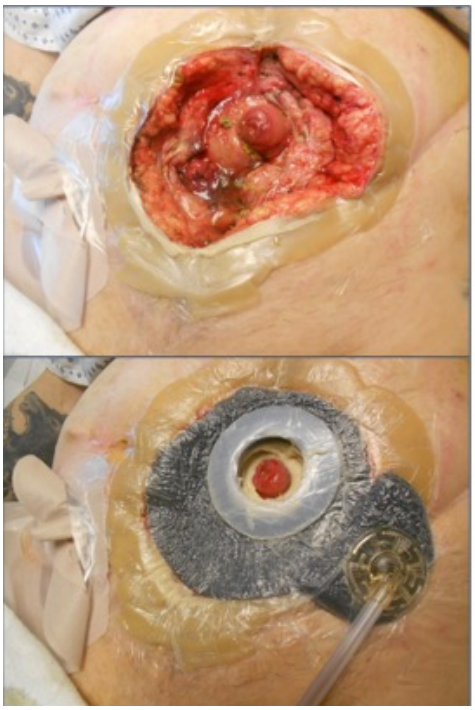
Background: Patients with complex abdominal wounds complicated by fistulas or difficult-to-pouch ostomies are rare but utilize a significant amount of healthcare resources due to effluent leakage. Persistent leakage causes skin breakdown and delays wound healing, which can tax patients and providers by forcing them to find creative ways to manage the wound. It can also result in cellulitis and readmission to the hospital or leave patients bound to a care facility. Skin grafts can accelerate the healing of open wounds. However, wounds around fistulas and ostomies are typically not suited for skin grafting due to the risk of effluent contamination.

Objective: In this case series, we describe a novel surgical technique to avoid effluent contamination of skin grafts on wounds around fistulas or ostomies.

Method: Our hospital is a regional referral center for complex, chronic abdominal wounds. To better manage these patients, we developed RISP (Revise, Isolate, Skin Graft, and Pouch). First, the wound bed around the fistula or ostomy is revised to prepare for skin grafting per standard protocol. A skin graft is harvested and placed on the wound bed, around the fistula or ostomy. The graft is covered with non-adherent dressings and bolstered by negative pressure wound therapy foam. An isolation device seals around the fistula or ostomy and protects the skin graft by allowing effluent to flow into an attached pouch. Dressings and isolation devices are changed every 3-5 days. At the time of submission, this technique had been used for 10 patients.

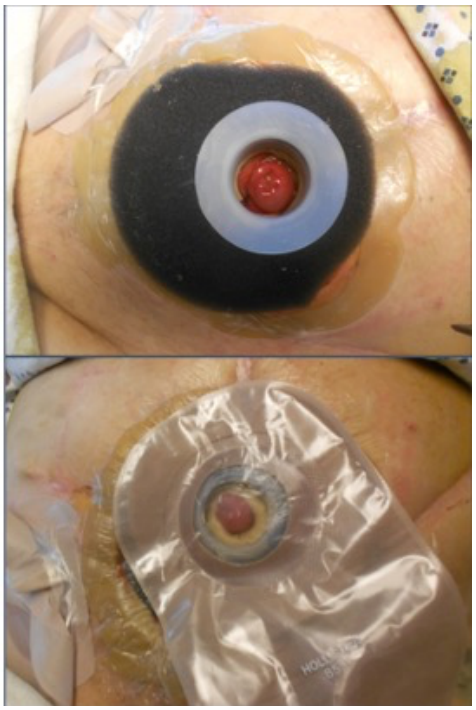
Results: The 10 patients (5 female and 5 male) ranged in age from 39 to 80 years. Co-morbidities included diabetes, malnutrition, CKD, infection, IBD, obesity, coagulation disorders, and poly trauma. Isolation devices with negative pressure foam dressings effectively sealed the effluent away from the newly placed skin grafts (Chart). Skin graft take and wound healing occurred for all patients. 9 patients transitioned to a standard ostomy pouch system for effluent management and discharged home.

Conclusion: This small case series demonstrates that skin grafting around fistulas and ostomies is feasible with the use of isolation devices and standard negative pressure wound therapy bolster dressings. Grafting enables healing to occur so that standard ostomy appliances can be used while these patients await final revision of their fistula or ostomy. Additionally, grafting reduces the risk of skin breakdown and cellulitis, allowing patients to discharge home rather than remain in the hospital or a care facility.



RISP

- Revise
- Isolate
- Skin Graft
- Pouch



Presentation #4 | Clinical Science | General Surgery

THE BENEFITS OF LOCAL ANESTHESIA USED IN MASTECTOMY WITHOUT RECONSTRUCTION

Aida K. Sarcon, Wenxia Zhang, Amy C. Degnim, Rebecca L. Johnson, William S. Harmsen, Amy E. Glasgow, James W. Jakub

Presenter: Aida Sarcon MD Mayo Clinic

Background: The opioid epidemic has driven interest in local anesthesia to reduce opioid use for postoperative pain control, but there is a lack of data evaluating local anesthetics and their postoperative benefits.

Objective: To determine if local anesthesia administered during mastectomy without reconstruction improves postoperative pain, oral morphine equivalents (OME), postoperative nausea/vomiting, and length of stay (LOS) in the post anesthesia care unit (PACU) or in the hospital.

Method: Single institution retrospective review of female patients who underwent mastectomy without reconstruction from 2014 to 2019. Data were collected and analyzed on the regimen of intraoperative local anesthesia, age, BMI, ASA score, maximum visual analogue pain scale (VAS) score on day of surgery and postoperative day (POD) 1, intraoperative and in hospital postoperative OME and antiemetics, PACU and hospital LOS, and surgical characteristics (i.e. bilateral or unilateral mastectomy, type of axillary surgery, and closure technique). Statistical analysis was performed using univariate and multivariate analysis (MVA).

Results: A total of 712 patients were included. Of the 712 patients, 63 (8.8%) received bupivacaine, 512 (72%) patients received liposomal bupivacaine, and 137 (19%) received no local. Ninety-five percent of patients were discharged on POD1 with a mean hospital LOS of 23 hours. Liposomal bupivacaine use increased from 2014 to 2019. Aside from year of surgery, the major factors associated with use of a specific local anesthetic regimen were the surgeon and extent of axillary surgery. Compared to no local, fewer patients used postoperative opioids if intraoperative local anesthesia was administered (76% vs 87.6%; p=0.003). Compared to patients without, those with local had shorter mean LOS in PACU (95 vs 87 min; p= 0.02), lower mean intraoperative OME (96 vs 106; p= 0.0001), and lower mean postoperative OME per hour (1.4 vs 1.8 p= 0.001).

The mean postoperative OME per hr was 1.4 for liposomal bupivacaine, 1.8 for bupivacaine, and 1.8 for no local, which for a 24hr period translates to 22.4 mg, 28.8 mg, and 28.8 mg of oxycodone, respectively. MVA accounting for age, BMI, ASA level, laterality, closure, and axillary surgery revealed both a significantly lower OME per hour with liposomal bupivacaine compared to no local (least square mean of 1.43 vs 1.91 OME per hour; p=0.002), and to bupivacaine (1.43 vs 1.93; p=0.02). Pain scores did not differ by local anesthetic use on POD0

and POD1 with univariate analysis, but MVA showed lower POD1 scores for the liposomal bupivacaine group (p=0.049). The use of local anesthetic was not associated with postoperative antiemetic use or LOS in the hospital.

Conclusion: In this retrospective series of patients undergoing mastectomy without reconstruction, the use of local anesthetics was associated with reduced hospital opioid consumption and increased likelihood of not using any opioids in the postoperative period. Furthermore, OME per hour was significantly lower with the use of liposomal bupivacaine. However, given limitations and bias from the retrospective nature of the data, a prospective study is warranted to determine the optimal anesthetic regimen for patients undergoing mastectomy without reconstruction.