Lignin Composites with Oxygen Generation and Antioxidant Properties Improve Diabetic Wound Healing

Nabila Anika MD
Baylor College of Medicine

Introduction/Background
Non-healing diabetic wounds are a major clinical problem with few targeted treatments available to promote wound healing. Impaired neovascularization, increased levels of reactive oxygen species (ROS), chronic low-grade inflammation and hypoxia are associated with diabetes, which disrupt mechanisms of wound healing. We engineered novel lignin-based (a natural antioxidant from lignocellulose) composites with ROS-scavenging and oxygen-releasing properties and hypothesized that they enhance neovascularization and attenuate inflammation to promote diabetic wound healing.

Methods:
Thiolated lignosulfonate (TLS) was covalently conjugated to methacrylated gelatin (GelMA). Sodium lignosulfonate (SLS) nanoparticles encapsulating calcium peroxide (CPO) were developed. Test groups included, Untreated (UNTX), GelMA, GelMA+TLS (TLS), GelMA+TLS+SLS without CPO (CPOc), and GelMA+TLS+SLS with oxygen releasing CPO (CPO). Mouse dermal microvascular endothelial cell branching on the lignin composites was tested in vitro by seeding 150k cells/sq. cm. In vivo, 6mm stented skin wounds in diabetic (db/db) mice were treated on day 0 following wounding and were harvested at d7 and d14 post wounding and examined for epithelial gap, granulation tissue (HandE), endothelial cells and vessels (CD31), macrophages (F4/80, CD206), VEGF and HIF1a expression. p values by ANOVA.

Results:
The dual function of CPO lignin composites promoted endothelial cell branching and their reorganization into capillary-like network formation ($p<0.05$) and corrected high glucose-induced changes in their VEGF and HIF1a expression in vitro. In db/db skin wounds, CPO lignin composites promoted granulation tissue deposition and capillary lumen density at d7 ($p<0.05$). Histological staining showed reduced VEGF expression in hyperproliferative leading epidermis of CPO-treated wounds at d7, but quantification of VEGF in the homogenized wound tissue using immunoblotting showed an increase in the VEGF expression at d7, suggesting dermal angiogenesis is promoted by CPO lignin composites in diabetic wounds. Interestingly, CPO-lignin treatment decreased HIF1a expression and macrophage infiltration. The effect of treatment at d14 showed visibly improved healing in CPOc and CPO wounds from gross images, which was supported by robust granulating wound bed in representative HandE stained wounds sections, along with an increase in CD31+ lumens noted at d14 with CPO lignin composites.

Conclusion
Engineered lignin biomaterials with multiple wound healing-promotive functions, including pro-angiogenic, sustained oxygenation and ROS–scavenging properties can synergistically correct diabetes-associated cell and wound microenvironmental impairments to promote wound healing.

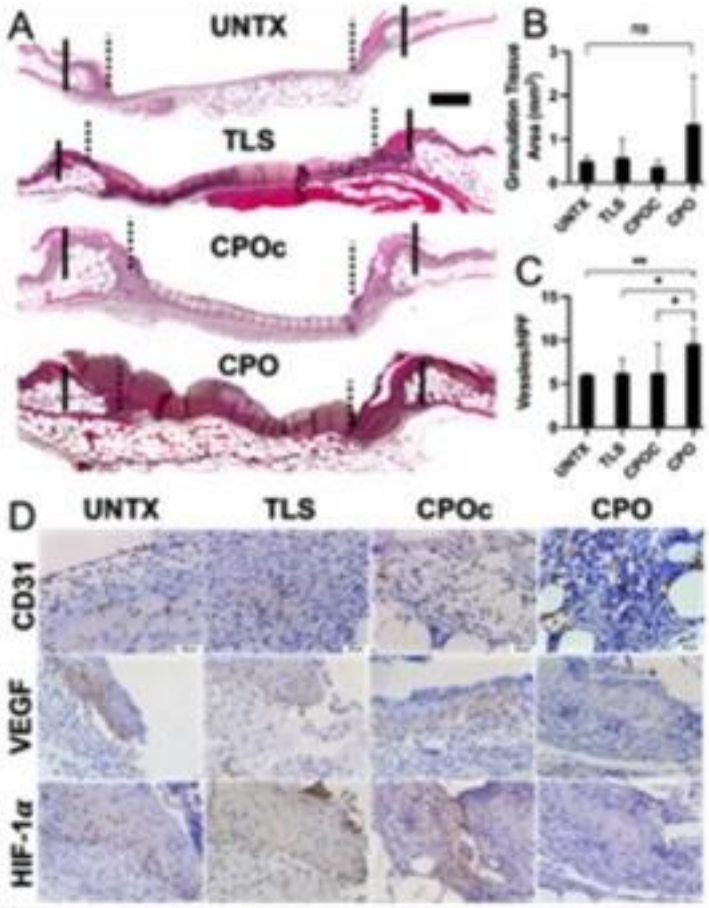


Figure 1. Wound healing in db/db mice. 6mm wounds in 8 wk old mice with blood glucose>350mg/dl were treated with lignin composite TLS, CPO or CPOc immediately after wounding. (A-B) H&E staining of wound sections at day 7 show that as compared to untreated (UNTX) wounds, wounds treated with lignin composite CPO appeared to have more granulating tissue. (C) CD31 staining of wound sections showed a significant increase in lumen density in CPO wounds at day 7. (D) Staining of day 7 wounds sections with antibodies against CD31, VEGF and HIF-1α. *$p<0.05$ ANOVA, Tukey's *post hoc* analysis, n=4 mice wounds/group.

The SAFIR Houston model: Comprehensive local surveillance to identify vulnerable populations and risk factors for pediatric firearm injury prevention

Jana DeJesus MD
University of Texas Medical Branch - Galveston

Introduction/Background
Injuries from firearms are now the leading cause of injury death among children. Currently, there are no collaborative local or national surveillance systems in place to monitor firearm-related injuries. The aim of this study is to propose and institute a comprehensive local surveillance model in order to guide targeted injury prevention efforts.

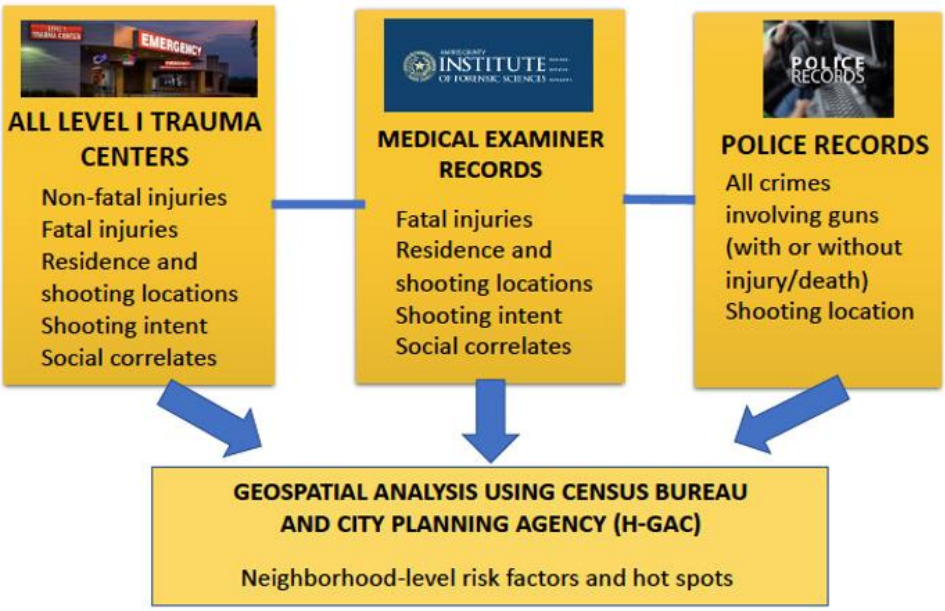
Methods:
The Surveillance To Assess for Firearm Injury and Risks (SAFIR) model (Figure 1), which integrates trauma center, medical examiner, and crime data regarding pediatric fatal and non-fatal firearm injuries (0-17 years) in a large Texas county (Harris County) was developed to study firearm-related events between 2018-2020. Crude rates were calculated using estimates per 100,000 persons in the population. Descriptive statistics and multinomial logistic regression were used to describe the relationship of factors to the injuries.

Results:
A total of 484 pediatric firearm injuries occurred over the 3-year period. Injuries from assault were most common (6.8/100,000), followed by unintentional (2.3/100,000) and suicide/self-harm (0.8/100,000). Black children (30.0/100,000) and males (20.3/100,000) had the highest crude rates for all injury types, most commonly due to assault. Compared to children injured from assault, children who suffered unintentional injuries were more likely to be younger (OR: -0.16, $p<.001$) and White non-Hispanic compared to Black non-Hispanic (OR: 1.92, $p<.001$); however, no difference was noted in gender ($p=0.90$). Compared to assault injuries, suicides were more likely to be female (OR: 1.37, $p=.005$) and White non-Hispanic when compared to Black non-Hispanic (OR:3.52, $p<.001$), but no difference was noted in age ($p= 0.29$). Unintentional injuries and suicides were more likely to occur at home. Suicides were more common in suburban regions, assault in the urban centers, and unintentional in both.

Conclusion
This model can provide comprehensive local surveillance to assess for epidemiologic and sociodemographic risk factors for pediatric firearm injury, which are vital to determine effective strategies for injury prevention.

THE SAFIR HOUSTON MODEL

(SURVEILLANCE TO ASSESS FOR FIREARM INJURY AND RISKS)



Impact of Timing of Decompressive Craniectomy on Outcomes in Pediatric TBI

Ryan Morgan BS
Texas Tech University - Lubbock

Introduction/Background

Decompressive craniectomy (DC) can be utilized in the management of intracranial hypertension in the setting of severe traumatic brain injury (TBI). Previous studies indicate that early DC (< 24 hours) may have potential benefits regarding mortality and long-term outcomes in adult populations. It remains unclear, however, if these benefits translate to pediatric patients. Further, the literature is limited in the risk assessment and prevention of the many complications that can occur post DC, particularly in the prevention of post traumatic hydrocephalus (PTH) and subdural fluid collections.

Methods:

This is a multicenter retrospective review over a 10-year period across two medical centers of patients ages 1 month - 18 years who underwent DC for TBI. Patients were stratified as acute (24 hours) based on timing to DC. Primary outcomes were Glasgow Outcome Scale (GOS) at discharge and 6-month follow up as well as complication rates. Secondary outcomes were PTH rates and evaluation of drain usage after DC.

Results:

A total of 47 patients fit the inclusion criteria: 26 (55.3%) were male with a mean age of 7.87 ± 5.87 years and admission Glasgow Coma Scale (GCS) of 5.83 ± 3.76. Overall mortality was 31.9% (n=15). When evaluating timing to DC, 36 (76.6%) patients were acute and 11 (23.4%) were subacute. Acute DC patients presented with lower GCS (5.02 ± 2.97) compared to subacute DC (8.45 ± 4.91) (p=0.030). Timing of DC was not associated with GOS at discharge (p=0.938), 3-month follow-up (p=0.225), 6-month follow-up (p=0.074), or complication rate (p=0.505). Post operative drains included external ventricular drain (EVD) in 55.3% (n=26) of patients and subgaleal drains in 82.9% (n=39) of patients. The rate of PTH following DC for both groups was 6.4% (n=3).

Conclusion

Although patients selected for early DC had more severe injuries at presentation, there was no difference in outcomes. Optimal timing of DC requires a multifactorial approach considered on a case-by-case basis. Furthermore, hydrocephalus rates following DC may be influenced by usage of post operative EVD, subgaleal drains, and early cranioplasty.

Sexual Differences in Clinical Outcomes of Neonates with Congenital Diaphragmatic Hernia

Oluyinka Olutoye II MD, MPH
Baylor College of Medicine

Introduction/Background

Congenital diaphragmatic hernia (CDH) is a morbid disease that leads to pulmonary hypoplasia and pulmonary hypertension (PH). Sex-based differences have been described in other neonatal pulmonary diseases but have not been investigated in CDH-PH. We sought to examine sex-based differences in CDH outcomes.

Methods:

A single-center retrospective cohort review CDH patients presenting to our institution between 4/1/2011 and 4/1/2021 was performed. Patients status post fetoscopic endoluminal tracheal occlusion, with multiple congenital anomalies or congenital heart disease requiring surgical intervention, along with those diagnosed with trisomy's 13, 18, or 21 were excluded. Demographics, perinatal outcomes, and echo reports outcomes were collected. Data were analyzed with Fisher's exact test, t-tests, Wilcoxon rank sum test, and log-rank test where appropriate.

Results:

Ninety-seven patients (66 male, 31 female) were included. There was no difference in the prenatal predictors, observed to expected fetal lung volume (p=0.08) and percent liver herniation (p=0.62), between males and females. Males demonstrated increased ECMO use (p=0.007) and mortality (p=0.02) when compared to females. Males were more likely to die or be discharged on pulmonary hypertension medications (p=0.006). There was no difference between length of mechanical ventilation, tracheostomy, or length of stay between males and females. Pre-repair echocardiograms were obtained for 88 patients (61 male, 27 female). Males more commonly demonstrated right to left or bidirectional shunting through the PDA (p=0.009). Ten patients exhibited isolated left ventricular dysfunction that persisted following hernia repair, all of whom were male.

Conclusion

Herein we report previously unreported sex-based differences in CDH outcomes with males exhibiting worse prognosis in PH, morbidity and mortality Further understanding the fundamental mechanisms in this clinical phenotype may lead to precision-tailored therapies for CDH-PH that has potential to improve patient outcomes.

	All CDH	Males	Females	p-value
Number of Neonates	n=97	n=66	n=31	
Mortality[1]	16 (16.5)	15 (22.7)	1 (3.2)	0.018*
ECMO Use[1]	38 (39.2)	32 (48.5)	6 (19.4)	0.007*
Tracheostomy Placement[1]	6 (6.2)	5 (7.6)	1 (3.2)	0.661
Mechanical Ventilation Days[2]	16 [8, 33]	16 [8, 38]	15 [8, 30]	0.883
Oxygen Days[2]	38 [15, 74]	31 [12, 74]	38 [19, 86]	0.212
Length of Stay, days[2]	51 [31, 99]	51 [32, 102]	52 [30, 83]	0.969
Pre-Repair Echo				
Presence of PDA[1]	n=88 79 (89.8)	n=61 54 (88.5)	n=27 25 (92.6)	0.716
PDA R → L or BiDirectional[1]	n=79 65 (82.3)	n=54 49 (90.7)	n=25 16 (64.0)	0.009*
Data are presented as (n, %) or median [interquartile range (IQR)] *Denotes statistical significance. 1.Fisher's exact test 2. Wilcoxon rank sum test.				

Outcomes of Same-Day Discharge Following Appendectomy for Pediatric Patients with COVID-19

Vikas Gupta MD
University of Texas Southwestern Medical Center

Introduction/Background
The use of same-day discharge protocols for uncomplicated appendicitis has been established at multiple children's hospitals. These protocols are effective in reducing hospital length of stay, bed and staff utilization, and overall healthcare costs. The safety of applying these protocols to COVID-positive pediatric patients with appendicitis remains undescribed. The aim of this work was to determine whether hospital discharge of pediatric patients with COVID-19 infection within 24 hours following uncomplicated laparoscopic appendectomy was feasible and safe.

Methods:
We performed a retrospective chart review of patients who underwent appendectomy for acute, uncomplicated appendicitis at our institution from January 1, 2020 to January 31, 2022 and were discharged within 24 hours after surgery. After pre-operative COVID-19 testing, patients were grouped based on their test status: COVID-negative (CovN) or COVID-positive (CovP). Primary outcomes included non-routine clinic follow-up visits within 7 days and hospital readmissions or need for further related procedures within 30 days. Secondary outcomes included time to surgery, time in the operating room (OR), total anesthesia care time, oxygen saturation values and length of stay in the post-anesthesia care unit (PACU), and time to discharge.

Results:
During the study period, 2,763 patients underwent laparoscopic appendectomy. Of these, 1,795 (1,711 CovN, 84 CovP) were discharged within 24 hours of appendectomy and were included in our analyses. The mean age of the cohort was 11.0 ± 3.6 years, and 61.1% of patients were male. There was no significant difference in age, sex, race, ethnicity, or BMI percentile (all $p>0.05$) between CovP and CovN patients. The rate of non-routine follow-up visits was 4.3% vs. 2.4% in the CovN and CovP groups, respectively ($p=.579$). The readmission rates at 30 days were 5.8% and 2.4% in the CovN and CovP, respectively ($p=.231$). There was no difference in the number of children undergoing additional procedures within 30 days following appendectomy based on COVID status (CovN 0.8%, CovP 1.2%, $p=.514$). Of these, only six patients in the CovN group and one in the CovP group underwent procedures related to their history of appendicitis ($p=.285$). Table 1 shows secondary outcomes; time to OR from hospital presentation, total OR and anesthesia time, and time in PACU were longer for CovP than CovN patients.

Conclusion
Same-day discharge after laparoscopic appendectomy for uncomplicated appendicitis in CovP pediatric patients is associated with similar post operative outcomes as CovN patients. Despite concerns about peri-operative complications for CovP patients, data from our center suggest that a subset of CovP but asymptomatic pediatric patients can be safely discharged within 24 hours after surgery and general anesthesia.

Secondary Outcome Measures				
	Cohort (n = 1795)	**COVID-negative** (n = 1711)	**COVID-positive** (n = 84)	
Time to OR (hours)	11.1 ± 5.9	10.9 ± 5.8	14.1 ± 6.7	*p*<.001
Time in OR (minutes)	63.0 (55.0-73.0)	62.0 (54.5-72.0)	73.0 (56.5-86.3)	*p*<.001
Total anesthesia care time (minutes)	67.0 (58.0-78.0)	67.0 (58.0-77.0)	79.0 (63.8-98.3)	*p*<.001
Time from procedure end to extubation (minutes)	5.0 (3.0-8.0)	5.0 (3.0-8.0)	6.0 (3.0-10.0)	*p*=.318
First O_2 sat value in PACU (%)	98.0 (96.0-99.0)	98.0 (96.0-99.0)	97.5 (96.0-99.0)	*p*=.920
Last O_2 sat value in PACU (%)	96.0 (95.0-97.0)	96.0 (95.0-97.0)	97.0 (95.0-98.0)	*p*=.089
Time in PACU (minutes)	39.0 (29.0-53.0)	40.0 (29.0-53.0)	25.0 (15.0-40.5)	*p*<.001
Time to discharge (hours)	2.9 (1.6-6.2)	2.9 (1.6-6.1)	2.8 (1.6-6.6)	*p*=.872

Table 1: Additional outcome measures. Data presented as mean ± SD or median (IQR), as appropriate. Statistical analysis performed using Student's t test, Kruskall-Wallis test, Fisher's Exact test, and Chi-squared analysis as appropriate.

Abbreviations: O_2 sat: Oxygen saturation, OR: operating room, PACU: post-anesthesia care unit

Abstract| Surgical Education

Utilizing a Student-Ran Call Clinic to Enhance Post-Discharge Care of Post-Operative Patients

Devin Shah BA
University of Texas Southwestern Medical Center

Introduction/Background

Post-operative patient safety in the post-discharge period requires high-quality transitional care. Telephone calls facilitate post-operative care and allow for early recognition of surgical complications. Student on surgical rotations rarely engage in the transitional care of patients whom they treated inpatient. We developed a student-run call clinic to enhance student participation in the transitional care of discharged post-operative patients and practice handoffs.

Methods:

Surgical students piloted an activity performing telephone calls to discharged post-operative patients. Students reviewed patient records and used call scripts to screen for warning signs of surgical complications. Flagged patients were immediately escalated to a surgical specialist. Patients without warning signs were interviewed for post-operative care concerns including pain control, medications, wound care, and follow-up. Students performed handoffs to surgical specialists using structured communication. Students recorded encounter information and handoffs in a call log. The call logs were used for analysis.

Results:

14 students called 30 patients during the pilot. All patients were contacted within two calls. 53.3% of patients had questions about post-operative care. One patient was escalated for reporting warning signs. Students provided 70% of patients with post-operative care information. 20% of encounters were referred to the surgical clinic or specialist for further assistance.

Conclusion

A student call clinic may augment post-discharge care of surgical patients, provide opportunities for students to practice teamwork competencies including structured communication, and increase student participation in the transitional care of their patients. Further identification of barriers and enablers to acceptability, feasibility and fidelity of student efforts may improve patient safety and surgical outcomes.

Thematic Analysis of Patient Questions, Student Instructions, and Referred Questions

Themes	Number of Encounters	Percentage of Encounters
Patient Questions	*16*	*53.3%*
Activity Limitations	3	10%
Follow-Up	8	26.7%
Pain Control	4	13.3%
Expected Recovery	1	3.33%
Medications	1	3.33%
Wound Care	3	10%
Student Provided Instructions	*21*	*70%*
Pain Control	3	10%
Wound Care	3	10%
Activity Limitations	2	6.67%
Follow-Up Information	20	66.7%
Return to ED/Clinic Precautions	7	23.3%
Questions Referred to Clinic or Specialist	*6*	*20%*
Medication Instructions	1	3.33%
Reschedule Follow-Up	2	6.67%
Schedule Follow-Up	1	3.33%
Activity Limitations	1	3.33%
Referrals	1	3.33%

Attending and Resident Expectations Compared with Resident Confidence Regarding PGY Competency for Laparoscopic Cholecystectomy

Justine Broecker MD
University of Texas Southwestern Medical Center

Introduction/Background
Laparoscopic cholecystectomy (LC) is defined as a core operation for which every graduating surgical resident must demonstrate proficiency; however, progression towards such proficiency is not defined or standardized. A curriculum to facilitate and standardize competency is needed and in the process of being developed nationally; however, many barriers to achieving competency based education currently exist including agreement of expected step-wise progression. Current expectations regarding resident competency for LC is relatively unknown. Our purpose was to survey attendings' and residents' expectations and confidence performing steps of LC.

Methods:
In this exempt-approved study, attendings and residents within the general surgery department of three sites of Mayo Clinic (Rochester, Arizona, Florida) were recruited to take an online anonymous survey. A total of 28 residents (9 PGY-1, 5 PGY-2, 4 PGY-3, 2 PGY-4 and 7 PGY-5) and 22 attendings completed the survey.

First, participants rated each step of the LC regarding when they expected residents of each PGY to be able to competently perform the step. Next, residents were asked to rate their confidence in performing each step.

ANOVA was used to compare expectations of residents versus attendings as there were more than 4 levels of expectations.

Results:
Almost all residents/attendings expected PGY-4 and PGY-5 residents to be able to dissect cystic structures; however, 100% of PGY-4 and 57% of PGY-5 residents felt confident performing this step. Expectations differed amongst attendings as well as between attendings and residents regarding performance and progression especially for more junior residents. For example, almost no residents or attendings expected a PGY-1 to be able to dissect cystic structures whereas 57% of residents and 32% of attendings believed a PGY-2 should be competent in this step($F(1,48)=5.32, p=0.02$). However, only 16% PGY-2 residents felt confident in performing this step. Additional significant disagreements between residents and attendings existed about whether a PGY2 should be expected to perform abdominal access($F(1,48)=4.24, p=0.04$), clip cystic structures ($F(1, 48 = 8.77, p = .005$), and dissect the gallbladder($F(1,48)=5.2, p=0.02$).

Conclusion
Significant disagreements exist amongst, and between, attendings and residents within a multi-site single institution regarding step-wise progression of expected competencies per PGY-year for LC. In addition, our results demonstrate that residents may not feel confident in the steps they are expected

to perform. This lack of consensus may represent a barrier to the development of a competency based curricula within general surgical education.