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A Retrospective Observational Study of Maximal Enteral Nutrition Rates in a Burn Patient Population

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A RETROSPECTIVE OBSERVATIONAL STUDY OF MAXIMAL ENTERAL NUTRITION RATES IN A BURN PATIENT POPULATION

by

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Research Focus. Enteral nutrition (EN) is frequently interrupted in the critically ill patient, which can lead to nutritional deficits and severe weight and lean body mass loss. Increased EN rates are being used more frequently to account for these interruptions. This study examined the maximum hourly EN rate (MAX rate) received by each subject and evaluated outcomes and tolerance in an effort to determine if there is a maximum threshold for the EN rate in this population.

Research Methods. This retrospective observational study was conducted on an adult population admitted to a major burn center during a three year period who received EN and had ≥20% total body surface area (TBSA) burned requiring excision. Demographics, treatment, and outcomes data were collected during the MAX rate that each subject received and were analyzed with descriptive and comparative statistics. The gastrointestinal (GI) intolerance data examined included emesis, residuals ≥500 mL, aspiration, ≥1 L stool output in 24 hours, and necrotic bowel during or after MAX rate. IRB approval was obtained.

Research Results/Findings. Data were collected on 151 subjects with 48% ± 18% TBSA burn who were 33 ± 14 years old and met the inclusion criteria. The average MAX rate ordered and received was 154 ± 45 mL/hr. The factors that predicted mortality in this study were burn size ($p = <0.001$), age ($p = <0.001$), and the total number of GI intolerance symptoms per subject during the MAX rate ($p = 0.011$). The MAX rate had a weak correlation with mortality and with any individual type of GI intolerance (all $R^2 <0.05$). MAX rate also had a poor correlation with the total number of GI intolerance symptoms per subject during MAX rate ($R^2=0.01$). Pressor agents running during the MAX rate in 15% of the subjects (n=23). Subjects who were on pressors during the MAX rate had significantly higher residuals [445 (143, 525) mL vs. 140 (0,340) mL] than subjects who were not on pressors during the MAX rate.

Conclusions from Research. The total number of GI intolerance symptoms experienced per subject was a predictor of mortality, but the MAX rate was not associated with increased GI intolerance symptoms. Pressor use during MAX rate was associated with the total number of different types of GI intolerance symptoms experienced per subject and with mortality. There were no strong correlation between increase in MAX rate and incidence of negative outcomes, therefore a definitive MAX rate could not be established.

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GLOSSARY OF ABBREVIATIONS, TERMS, AND VARIABLES

age measured in years

aspiration a yes/no question of was aspiration recorded in the physician notes during the time the subject was receiving the MAX rate

emesis during the MAX rate a yes/no question of did the subject had emesis recorded by the physician or nurse while receiving the MAX rate

enteral Nutrition (EN) the provision of nutrients into the gastrointestinal tract through a tube or catheter.

enteral nutrition formula created by separate nutrient sources or by modified existing formulas.

feeding tube placement post-pyloric prior to beginning the MAX rate a yes/no question of did the subject have a feeding tube placement past the pylorus prior to beginning the MAX rate

gastric residual volume (GRV) a volume of food or partially digested food and digestive enzymes left over in the stomach from a previous feeding measured in mL

gender defined as male or female

height (cm) pre-injury height measured in centimeters

high stool output a yes/no question of did the subject have a stool output >1L in 24 hrs while receiving the MAX rate

highest GRV(mL) highest GRV measured during the MAX rate

ICU intensive care unit

initial predicted REE using the Carlson equation this was the initial REE calculated upon admission to the USAISR

MAX rate maximum enteral feeding flow rate ordered and received, measured in mL/hr

military vs. civilian the subject was admitted to the USAISR as either an active duty military member or a civilian

mortality survival/non-survival at time of discharge from the hospital

necrotic bowel after the MAX rate a yes/no question of did the subject have necrotic bowel diagnosed upon completion of receiving the MAX rate

necrotic bowel during the MAX rate a yes/no question of did the subject have necrotic bowel diagnosed while receiving the MAX rate

necrotic bowel during or after the MAX rate a yes/no question of did the subject have necrotic bowel diagnosed during the MAX rate or diagnosed upon completion receiving the MAX rate

pre-injury weight (kg) documented body weight pre-injury or the most recent known body weight pre-injury measured in kilograms

pressors during the MAX rate a yes/no question of if the subject received pressor agents while receiving the MAX rate; type and rate of these pressors were also recorded

promotility agent at the start of the MAX rate a yes/no question of was the subject on a promotility agent at the initiation of the MAX rate

promotility agent during MAX rate a yes/no question of did the subject have a promotility agent started during the MAX rate

TBSA total body surface area

total number of GI intolerance symptoms per subject scored on a scale of zero to four, with zero indicating that the subject experienced none of the types of GI intolerance symptoms listed above during the MAX rate and four indicating that the subject experienced all four types of GI intolerance symptoms during the MAX rate

total number of hours subject received the MAX rate the specific amount of time measured in hours a subject received the MAX rate

types of GI intolerance symptoms aspiration, necrotic bowel, emesis, high stool output

Chapter 1: Introduction

Statement of the Problem

Thermal injury provokes the body's defense mechanisms causing a cascade of reactions immediately following the injury. As part of the inflammatory response that occurs, all systems in the body will compensate accordingly due to the influx of hormones serially triggering a hypermetabolic state.[1] The body's energy needs are much higher post injury than usual baseline energy requirements.[2-4] The initial concern is replacing fluid and electrolytes lost due to injury in order to prevent shock. Protein stores are depleted due to protein losses through open wounds and catabolism.

Carbohydrate has a protein-sparing effect on nutrient metabolism in burn patients. A.S.P.E.N. guidelines indicate that nutritional support should provide 20-25% of calories from protein, 60% of calories from carbohydrate, and 15-20% of calories from fat.[5]

The nutritional status of burn patients requires special attention during the course of their hospitalization to promote wound healing and prevent weight loss and lean body mass wasting. Even if they not intubated and are able to tolerate some oral intake, burn patients often require supplemental nutrition to help meet calorie needs. Prolonged, frequent interruptions in enteral nutrition (EN) could delay the recovery process due to the resulting caloric deficits,[6] making EN a high priority for recovery after severe burns. It is essential that further research be conducted on nutrition in burn patients to advance the medical knowledge in burn medicine.

Purpose of the Study

The primary purpose of this study was to determine if there is a maximal EN feeding rate (MAX rate) that can be established for burn patients. This was determined by examining negative outcomes, such as aspiration, elevated gastric residual volume (GRV), and necrotic bowel along with the MAX rate the subjects received.

While determining a MAX rate a short list of secondary questions was developed:

- Did subjects who had a higher mortality receive a higher volume or longer duration of the MAX rate than those subjects who survived?
- Was GI intolerance during the MAX rate related to any of the following factors: the MAX rate, duration of receiving the MAX rate, age, height, pre-injury weight, % total body surface area (TBSA) burn, predicted REE, post-pyloric placement of the feeding tube prior to beginning the MAX rate, or mortality?
- Did subjects who experienced emesis during the MAX rate have a greater number of GI intolerances than subjects who did experience emesis during the MAX rate?
- Did subjects who aspirated during the MAX rate have a greater number of GI intolerances than subjects who did not aspirate during the MAX rate?
- Did subjects who had GRV >500 mL during the MAX rate have a greater number of GI intolerances than subjects who did have GRV <500 mL during the MAX rate?
- Did subjects on promotility agents at the start of the MAX rate have less GI intolerances than subjects not on a promotility agent at the start of the MAX rate?

- Did subjects who had a new promotility agent added after the start of the MAX rate have less GI intolerances than subjects who did not have a promotility agent added after the start of the MAX rate?
- Did subjects who were on pressors during the MAX rate have less GI intolerances than subjects not on pressors during the MAX rate? Did subjects who had stool output >1L per day during the MAX rate have a greater number of GI intolerances than subjects who did not have stool volumes >1L during the MAX rate? Did subjects who had necrotic bowel during the MAX rate receive a higher MAX rate or receive the MAX rate longer? Was the duration of the MAX rate different in subjects who had necrotic bowel during the MAX rate than those subjects who did not have necrotic bowel during the MAX rate? Did subjects who had necrotic bowel during or after the MAX rate receive a higher MAX rate or have a longer duration at the MAX rate than those subjects who did not have necrotic bowel during or after the MAX rate?

Significance of the Study

The objective of this study was to establish if there was a MAX rate that burn patients could tolerate in order to aid in meeting caloric needs during the time EN is provided, working around frequent interruptions in EN.

Limitations of the Study

Due to the retrospective study design these additional factors and their possible effects on the tolerance of EN were not analyzed: additional medical complications post-operatively, blood pressure medications that may effect GI motility or contribute to large stool volume,

mechanical ventilation or intubation, *Clostridium difficile*, sepsis, mucormycosis, and additional systemic infections.

Chapter 2: Literature Review

Background

If adequate nutrition is not provided, weight loss is common after thermal injuries due to the prolonged heightened metabolic state and increased energy demands. [7] Nutrition intervention is a vital component for a successful recovery from severe burns . The nutritional needs of burn patients are very high, requiring 1.5-2 g/kg of protein per day, 2534 ± 738 kcal per day [4] 60% of calories from carbohydrate, and 15-20% of calories from fat.[5] In addition to elevated macronutrient needs, burn patients also have elevated micronutrient needs to promote wound healing and successful grafting after excision. A.S.P.E.N. recommends 5,000 IU of Vitamin A per 1,000 kcal of EN, 500mg of Vitamin C twice daily, 220mg of zinc sulfate, and additional non-specific supplementation of vitamins D, K, and folic acid. [5]

Thermal injury induces a hypermetabolic state, putting burn victims at high risk for malnutrition. Nutritional support must meet the high caloric needs to support the hypermetabolic state while also meeting the high protein needs necessary for wound healing. [7] Inadequate nutrition can result in severe weight loss, muscle wasting, poor wound healing, a weakened immune system, increased infection, and increased mortality. [7-11]

The physiology of the hypermetabolic state is directly related to a widespread inflammatory response in the body. Inflammation and increased cytokine levels caused by thermal injury activate the neuroendocrine and adrenal response in the hypothalamus resulting in a spike in catecholamine, glucagon, and cortisol levels; this triggers an explosive systemic response with an increase in oxygen needs and consumption, metabolic rate, temperature, protein catabolism, and lipolysis while simultaneously catabolizing lean mass and fat mass. [8]

Increased energy requirements are directly related to burn size and the increased production of stress hormones. [4,8,10,12]

The ebb and the flow phase of the hypermetabolic state are greatly affected by insulin levels. The ebb phase takes place during the first 48 hours post-burn and it is during this phase that the body has a decreased metabolic rate and decreased insulin levels. When the flow phase begins the increased metabolic state also begins. Hyperinsulinemia and hyperglycemia soon follows once the body enters the hypermetabolic phase.[13] since insulin acts as an anabolic hormone, burn patients are better controlled when they are on an insulin therapy regimen. [14] In addition, insulin therapy stimulates protein synthesis and transport of amino acids.[13,15]

There is an established relationship between a negative nitrogen balance and an increase in glucagon levels in the early phases of catabolism, which starts at post-burn days two and three. Glucagon levels drop back down to normal after the burn wound closes.[10,16-17]

Nutritional Needs of the Burn Patient

Nutritional needs are assessed using a variety of methods, including biochemical, anthropometrics, diet history, and clinical data.[10,12] Indirect calorimetry can also be used to determine energy needs. Shields et al. compared nine predictive equations to indirect calorimetry in order to determine which equation was the most accurate in determining the REE for the burn patient.[4] The nine predictive equations included: 30 kcal/kg, 35 kcal/kg, 40 kcal/kg, Harris-Benedict x 1.5, Carlson, Milner, Xie, Zawacki, and Curreri. Results showed that the Carlson and Milner equations provided the most satisfactory estimation of REE.[4]

Carbohydrate composition of EN formulas can affect how easily the EN is digested. While a majority of carbohydrates are easily digested, lactose remains the one exception in critically ill patients. It is not uncommon for patients to become lactose-intolerant post-burn

injury even if they did not have sensitivities to lactose prior to injury. Carbohydrate metabolism changes after burn injury to include elevated amino acid and alanine gluconeogenesis secondary to the hypercatabolic state. [10]

Fat content of EN formulas also needs to be determined carefully for the burn patient. High intakes of dietary fat can actually delay the healing process of burns due to lipids impairing immunological responses in the body. [8,12] Limiting lipid composition to 12-15% of non-protein calories yields the best results. Lipid composition less than 15% of non-protein calories has shown to improve respiratory function, shorten length of stay, and increase wound healing.[8,17]

Protein synthesis is one of the main focuses of nutritional support in burn patients. Protein needs are extremely high as protein is lost in urine and wounds.[8,12] the body is also in a state of enhanced gluconeogenesis. The primary substrates for the enhanced state of gluconeogenesis come from amino acids produced from muscle catabolism.[13] this provides energy for the open wounds, which is needed for healing to occur. Protein sparing is important in burn patients with nitrogen retention, therefore energy from carbohydrates is appropriate for burn patients. [5,8]

Glutamine is important for immune cells, muscle metabolism, and intestinal mucosal cells.[18] The provision of supplemental glutamine has demonstrated preservation of intestinal mucosal structure[18] and glutamine enriched diets are beneficial in reducing the cases of developed pneumonia and sepsis in poly-trauma.[19] In burn patients, glutamine supplementaion improves glutamine levels, increases protein synthesis, promotes wound healing, and improves nitrogen balance. [8]

Feeding Protocols and Flow Rates

The time frame for starting EN is also a critical component of the nutritional intervention. Initiation of early EN is associated with better outcomes in patients in a hypermetabolic state. Early aggressive EN decreased skeletal muscle catabolism in burned children. [20]

Preventing caloric deficits in burn patients is the key to successful nutrition intervention.[6] Maintenance of a functional gastrointestional (GI) tract in critically ill burn patients is a vital component of successful nutritional support. Initiating EN within one hour upon admission to the burn unit showed a lower incidence of sepsis and gut atrophy and a reduction in caloric deficit and protein catabolism when compared to beginning EN greater than one hour after admission. [9] Studies show that beginning supplemental nutrition immediately upon admission to the hospital helps to achieve positive nitrogen balance[21] and prevents ileus and pressure ulcers in severely burned patients.[22] Several different EN protocols have been evaluated to determine which has the least complications with the best outcomes. Rice et al. examined outcomes between initial trophic EN versus full EN during the first 6 days of hospitalization in patients with acute lung injuries (initiated at 25 mL/hr and if tolerated, advanced by 25 mL/hr until full caloric rate was reached, subjects on pressor agents were not excluded). Results showed that there was no significant difference in respiratory complications in patients given the full feeding regimen receiving 100% of their EN volume versus the trophic feeding regimen group.[23]

Spain et al. developed an infusion protocol for EN in a coronary or medical critical care unit starting feeds at 25 mL/hr advancing by 25 mL/hr every eight hours until reaching goal. When nursing staff was compliant with the protocol, patients achieved the EN hourly goal rate within 72 hours with minimal complications. [24] It was noted that when the protocol was physician ordered 82% of nursing staff was compliant. [24] Woien et al. tested a nutritional support

algorithm using a baseline of 20 mL/hr advancing the rate by 20 mL/hr as tolerated until goal EN rate was reached. When nursing staff followed the algorithm, patients reached target feeding goals within a 72-hour window. [25]

The American Society for Enteral and Parenteral Nutrition (ASPEN) and the Society for Critical Care Medicine (SCCM) have created EN protocols for the critical care setting. [2] These guidelines included initiating EN within the first 24-48 hours after admission, advancing to goal rate with in the next consecutive 48-72 hours, providing 50-65% of the goal calorie needs during the first week of hospitalization, and not holding EN for GRV less than 500 mL. [26-27]

A new enteral feeding protocol developed by Heyland et al, greatly improved the delivery of enteral nutrition in critically ill patients by 60.1%. The Protein-Energy Provision via the Enteral Route Feeding Protocol (PEP uP Protocol) was designed to initiate and maintain aggressive enteral nutrition in critically ill patients who are often hypocaloricly fed. [28] The PEP uP Protocol differs from other intensive care unit (ICU) feeding protocols in that it initiates enteral feeding using a 24 hour volume goal versus an hourly goal rate which provides the option to provide a trophic feed of a concentrated formula rather than a full feed of a polymeric formula.

This change also allows for a GRV to be set at 300 mL before enteral feedings are held by nursing staff. [28] This was a multicenter trial in Canada and tested in twenty four ICU's and sixteen control hospitals. Results of the PEP uP trial showed that patients hospitalized in facilities implementing the trial received 60.1% of their estimated calories from EN compared to 49.9% in control hospitals ($p=0.02$). Patients in this trial also received 61.0% of estimated protein needs compared to 49.7% in control hospitals ($p=0.01$). [28]

Gastrointestinal Intolerance of Enteral Feeding

GI tolerance of EN in critically ill patients is closely monitored by nursing staff in every ICU. A retrospective analysis was conducted on 1,888 mechanically ventilated patients in 167 ICU's globally to assess EN protocols and practices, specifically, how GI intolerance of EN was determined at each facility and what were the commonalities. [29] They examined high GRV's, large stool volume, abdominal distension, emesis, diarrhea, and reported discomfort. Results showed that the most common reason EN was interrupted was high GRV's, which were defined from a range of 50-500 mL based on the facility protocols. Results showed that intolerances of EN were good predictors that patients would receive less calories and protein during their stay, remain in the ICU for a longer period of time, and remain mechanically ventilated longer. [29]

Interruptions

Continuous EN is disrupted for various reasons, including high GRV, surgery, wound care, bathing, radiology, shock, and tube displacement. [30] A study including patients from a coronary ICU showed that only 14% of patients received their prescribed amount of EN, primarily because of interruptions.[24]

Following protocol and increasing feeding rates to make up for the caloric deficit due to these interruptions is key in a burn patient population since patients can quickly lose 10-20 pounds of lean body mass without displaying physical evidence of significant weight loss due to swelling from fluid resuscitation.[10] Research is needed to determine a MAX rate in the burn population in order to reach prescribed daily intake via EN.

The medical team at the research facility where this study was conducted was clinically uncomfortable giving MAX rates over 200 ml/hr although the caloric goal at times required higher MAX rates. However, it was noted that the staff was comfortable with boluses of higher

volumes beyond the continuous hourly rate. The purpose of this research was to investigate different MAX rates provided to burn subjects, along with any negative outcomes, such as aspiration, elevated GRV, and necrotic bowel to determine if a MAX rate threshold exists that avoids intolerance in order to promote the achievement of caloric goals in burn patients whose continuous feeding regimen can be frequently interrupted. The time period selected was during a time of a high rate of necrotic bowel.

Chapter 3: Research Methodology

Study Location & Population

The population of this study includes burn subjects who were admitted to the United States Army Institute of Surgical Research (USAISR) at San Antonio Military Medical Center (SAMMC) in Ft. Sam Houston, TX and was approved by the Institutional Review Boards (IRB) at both SAMMC and the University of the Incarnate Word.

Inclusion/Exclusion criteria

Data were collected from medical charts on subjects admitted from September 21, 2005 to July 31, 2008, who were at least 18 years of age, had burns requiring ≥20% TBSA excision and grafting, and required EN to meet nutritional needs. Other specific disease states were not excluded**.** Subjects were not excluded from this study unless they did not meet the inclusion criteria as listed above. Subjects who did not have EN initiated were not included.

Protection of Data (HIPAA)

Information was maintained in a secure database with access limited to principle investigators, associate investigators, and IRB approved personnel. Data was retained permanently to allow for follow up on outcomes. Data was stored on the USAISR password protected, firewall guarded network server. The data with patient identifiers was accessed at the USAISR and SAMMC and did not leave the premises.

The patient identifiers collected included the subject's name, age, medical record number, admission and discharge dates, and date of injury. This information was needed to access and verify the patient's medical records which may be located in different places. Subjects were identified by a medical record number and the medical record number was replaced with an assigned numerical value on the data collection sheet.

The main risk to subjects was loss of confidentiality. Human subjects were protected by the Health Insurance Portability and Accountability Act of 1996 (HIPAA) since the data collected were also part of their permanent medical records at SAMMC. To minimize this risk, any identifiers collected for this study were password protected in a secure drive as described.

Informed consent

No information sheet was required by the SAMMC IRB. There was minimal risk of disclosing identifying patient information during or after the study. Patient identity was protected as described previously. The waiver of authorization did not adversely affect the rights and welfare of the subjects. The data entered into the analysis were information routinely obtained during evaluation and treatment. Inclusion in the study did not put subjects at risk. Private health information was protected as described previously, therefore protecting the rights and welfare of the patients. No additional risks were imposed upon the subjects, as they were receiving the standard of care during this descriptive study.

It would not be possible to conduct the study without recording identifiers. The identifiers were needed to correlate data from different sources. Documenting consent would create an unnecessary link between the study and the subject for this minimal risk study.

Standard of Care and Clinical Practice Guidelines [3, 31-39]

The standard of care at the ISR was outlined in the USAISR Clinical Practice Guidelines. Execution of these guidelines for each patient was ultimately determined at the discretion of the attending physicians. The standard of care at the USAISR included evaluation by the burn team registered dietitian (RD). The RD estimated each patient's metabolic needs by several methods: the Carlson[33] and Milner[3] equations, metabolic cart studies, nitrogen balance studies, DEXA scans, weight loss when the edema resolved, and vitamin and mineral labs. The Carlson

equation[33] was used to calculate initial resting energy expenditure (REE) for patients with thermal injury upon admission. The Milner equation[3] was used after post burn day 30. The Carlson and Milner equations are as follows:

Carlson equation:
EER = [BMR x (0.89142 + {.01335 x TBSA})] x BSA x 24 x AF

Milner equation:
EER = [BMR x (0.247 + 0.0079 x TBSA -0.004 x PBD) + BMR] x 24 x BSA x AF

Harris Benedict Equation:
(Men) BMR = [66 + (13.7 x wt) + (5 x ht) – (6.8 x age)] x IF x AF
(Women) BMR = [665 + (9.6 x wt) + (1.8 x ht) – (4.7 x age)] x IF x AF

EER = Estimated Energy Requirement
BMR= Basal Metabolic Rate determined from Harris Benedict Equation[34]
TBSA = Total Body Surface Area burned (e.g. for 30% burn use 30)
BSA (m^2) = Body Surface Area $\sqrt{(Ht \times Wt) \div 3600}$
AF = Activity Factor
IF = injury factor
PBD = Post Burn Day

Since energy needs and REE changed throughout the recovery process from a thermal injury, REE was also validated by indirect calorimetry studies when available. Metabolic cart studies were routinely performed early in the morning before any daily activities began. These studies were conducted by the respiratory therapist or RD and the results were interpreted by the RD.

To estimate protein needs, patients were given 1.5-2.5 g/kg proportional to burn size until the results of the nitrogen balance study were available. Nitrogen balance studies were routinely conducted weekly for all patients with a ≥20-30% TBSA burn with a goal nitrogen balance of +2 to +4 grams per day. Urine collection was performed Sunday morning through Monday morning (24 hrs) to determine the patient's urine urea nitrogen (UUN) level. The Waxman equation was

used to calculate estimated nitrogen losses through the wound.[37] The equations for nitrogen balance and Waxman are as follows:

Nitrogen Balance:

Nitrogen g /day = (protein intake/ 6.25) – (UUN x 1.25 + 5 + *Waxman)

Waxman equation:

PBD 1-3: Nitrogen g /day = 0.3 x BSA x % TBSA burn
PBD 4-16: Nitrogen g /day = 0.1 x BSA x % TBSA burn
PBD >16: Nitrogen g /day = 0.1 x BSA x % TBSA burn open

PBD = Post Burn Day

Patients with a burn size of ≥20-30% TBSA had a jeujunal placement of a Dobhoff tube upon admission at the surgeon's discretion. Patients had serum vitamin and mineral levels checked as clinically indicated. Enteral feedings were routinely started at full strength at a rate of 20-25mL/hr and were advanced by 20-25ml/hr every 4-8 hours as tolerated until the determined goal rate was reached. Enteral feeds were to be discontinued upon going to the operating room and were resumed at the pre-surgical rate when returning to their room.

GRV's were monitored every 4 hours. Residuals ≥ 500mL were held and the physician was notified. Residuals ≥ 300mL were rechecked in 2 hours. If residuals ≥ 300mL continued to remain above 300mL, the tube feed was held for 4 hours and the GRV was rechecked. All residuals < 500mL were to be returned to the patient.

For all patients who were previously healthy and had no diagnosis of stroke, the standard of care was to advance the diet when the patient was alert, oriented, and able to take food and beverages by mouth. Diet advancement was monitored closely for any signs of intolerance. If for any reason a patient had difficulty swallowing with a nasogastric tube, a smaller tube was placed. If a patient was not tolerating thin liquids, liquids were thickened to assist with swallowing and

were closely monitored for diet advancement and tolerance. Chest films were monitored for any new infiltrates. All patients in the ICU on an oral diet were placed on a calorie count. These patients were not allowed to drink water, Gatorade, Kool-Aid, or caffeine containing beverages unless the diet order indicated these beverages were allowed.

The standard enteral formula was Peptinex DT® (1 Kcal/mL, 55.5 g protein/L). Standard modular protein was Propass® (Hormel Health Labs). GlutaSolve® (Nestle Nutrition) was the glutamine supplement. Not all subjects in the study were necessarily given the standard enteral formulas mentioned. Some subjects may have been given other enteral formulas available to the hospital based on the severity of their injuries and phase of recovery. The additional enteral formulas available in the hospital were various and dependent on the current contracts with outside vendors.

As previously mentioned, the medical team was clinically uncomfortable giving MAX rates over 200 ml/hr, even if caloric goal at times required higher MAX rates. There were no standard guidelines for MAX rates.

Data Collection

Both printed and electronic patient records were accessed for this study. Data sources included medical records, Essentris (CliniComp, Intel, San Diego, CA) CHCS (Science International Applications Corporation, McLean, VA) and the H-07-034 data viewer. Categorical data were summarized with yes/no answers or other appropriate verbiage. Categorical data included GRV >500 mL, emesis during the MAX rate, stool output >1 L in 24 hours during the MAX rate, aspiration during the MAX rate, necrotic bowel during the MAX rate, necrotic bowel after the MAX rate, necrotic bowel during or after the MAX rate, if the subject was on pressors during the MAX rate, the EN formula, feeding tube placement prior to beginning the MAX rate,

gender, military vs. civilian, promotility agent at the start of the MAX rate, promotility agent started during MAX rate, any type of GI intolerance symptoms, and mortality. The numerical data included age, height, pre-injury weight (kg), %TBSA burn, initial predicted REE, MAX rate (mL/hr), total number of hours subject received the MAX rate, highest GRV during the MAX rate (mL), and the total number of GI intolerance symptoms per subject.

Data Analysis: Statistics

Categorical data were summarized using incidence and percentages. Fisher's Exact tests or Chi-Square tests were used to compare two categorical data categories. The sample size determined whether the Fischer's Exact test or Chi-Square test was used. If the sample size produced results < 5 per group, a Fischer's Exact test was performed.[40]

Means and standard deviations or medians with inter-quartile ranges were used as summary statistics. These variables were analyzed against categorical data using the Wilcoxon test. The subjects were grouped by MAX rate and evaluated for incidence of categorical data and average numerical data. This created two continuous variables. Continuous variables from these groups as well as individual subjects were analyzed together for association using a linear regression where a high R^2 value (~ 1.0) represents a strong correlation and a low R^2 value (~ $\leq$0.01) represents a weaker correlation.

Logistic regression was performed to predict mortality. All p-values < 0.20 were considered for the model. Starting with a larger model, backwards elimination was used to remove all factors whose p-value was > 0.10. The final model included only significant factors.

Statistics were conducted using SPSS® (Version 19.0 Armonk , NY IBM corporation), Excel® (2010 Santa Rosa, CA Microsoft corporation), SAS® (Version 9.0, SAS institute INC

Cary, NC), and JMP® (Version 10, SAS institute INC Cary, NC). Significance was established when the p-values were <0.05.

Chapter 4: Results

There were 188 adult subjects who were admitted with at least 20% TBSA burn requiring excision during the time of this study; 19 were excluded from this analysis for receiving an oral diet and no EN, one was excluded for receiving TPN and not receiving any EN prior to death, and 17 died prior to the initiation of EN, TPN, or an oral diet. Table 1 describes the 151 subjects of the entire included population, who had an average of 48.3 ± 17.6% TBSA burn and who received an average MAX rate of 153.6 ± 45.2 mL/hr. Most of the subjects were men (93%) and most (69%) were in the military, with a mean age of 32.6 ± 14.0 years old.

Non-survivors were older and had a significantly larger % TBSA burn, higher estimated REE, higher maximum GRV, higher incidence of aspiration, higher incidence of necrotic bowel during and/or after the MAX rate, higher incidence of pressor use, lower incidence of emesis, and shorter stature; however, age, % TBSA burn, and number of intolerant factors were considered the only significant factors in predicting mortality using logistic regression. Survivors had 44 ± 15% TBSA burn, and those who died had 58 ± 20% TBSA ($p=<0.01$). Survivors were 31.0 ± 12.7 years old, and those who died were 36.3 ± 16.5 years old ($p=<0.134$). For every one year increment increase in age, the subject's mortality odds increased by 7% and for every 1% increase in burn size, mortality odds increased by 8% (Table 2).

Survivors experienced an average of 0.7 ± 0.8 types of GI intolerance symptoms during MAX rate, whereas those subjects who died experienced 1.0 ± 1.1 types of GI intolerance symptoms during MAX rate. This was not significantly different ($p=0.16$) using the Chi-Square test, but was found to be a significant factor for predicting mortality with logistic regression ($p=0.011$). For each additional GI intolerance symptom a subject experienced, their mortality odds increased by two fold (Table 2).

Table 1

Subject Characteristics and Outcomes

Characteristic	All (n=151)	Lived (n=106)	Died (n=45)	p-value
Women, n (%)	10 (7%)	4%	13%	
Men, n (%)	141 (93%)	96%	87%	0.031
Military	104 (69%)	73%	60%	0.130
Age, years	32.6 ± 14.0	31.0 ± 12.7	36.3 ± 16.5	0.134
Height, inches	69.5 ± 3.1	70.0 ± 2.9	68.5 ± 3.4	0.014
Weight, kilograms	82.3 ± 15.6	82.4 ± 13.4	82.1 ± 20.2	0.481
%TBSA[1] burn	48.3 ± 17.6	44.2 ± 15.0	58.2 ± 19.6	<0.001
Total number of GI intolerance symptoms per subject	1 (0,1)	0 (0,1)	1 (0,2)	0.126
Estimated REE[2] (kcal/day)	2669.5 ± 523.3	2577.0 ± 466.3	2892.5± 588	0.001
MAX[3] rate ordered (mL/hr)	153.6 ± 45.2	151.0 ±38.5	148.0 ± 54.3	0.762
Hours at MAX rate	60 (18,153)	76 (20,170)	41 (14,107)	0.065
Post-pyloric feeding prior to MAX rate	76 (50%)	53%	44%	0.371
Promotility agent at start of MAX rate	29 (19%)	23%	11%	0.872
Promotility agent added during MAX rate	22 (15%)	7%	33%	0.518
Pressors during MAX rate	22 (15%)	7%	33%	<0.001
Emesis during MAX rate	25 (17%)	21%	7%	0.277
Highest GRV[4] during MAX rate (mL)	160 (15, 390)	120 (3, 308)	275 (100, 500)	0.010
Stool output >1L/day during MAX rate	52 (34%)	32%	40%	0.356
GRV >500mL during MAX rate	19 (13%)	10%	18%	0.287
Aspiration during MAX rate	3 (2%)	0%	7%	0.025
Necrotic bowel during MAX rate	7 (5%)	2%	11%	0.014
Necrotic bowel after MAX rate	11 (7%)	2%	20%	<0.001
Necrotic bowel after or during MAX rate	18 (12%)	4%	31%	<0.001

Table 1 Definitions: [1]percent total body surface area burned, [2]resting energy expenditure, [3] maximum enteral feeding flow rate ordered and received measured in mL/hr, [4]gastric residual volume. Data presented as mean ± standard deviation, median (IQR) or n(%)

Table 2

Odds Ratio Estimations for Mortality

Effect	Point Estimate	95% Wald Confidence Limits	p-value
Age	1.073	(1.037, 1.110)	<0.001
% TBSA[1] burn	1.079	(1.046, 1.113)	<0.001
Total number of GI intolerance symptoms per subject	1.966	(1.165, 3.320)	0.011

Table 2 Definitions: [1]percent total body surface area burned

Pressors (vasopressin and dobutamine) were running during the MAX rate in 15% of the subjects. The average MAX rate during pressor use was 152.3 ± 57.2 mL/hr. Subjects who were on pressors during the time of the MAX rate had a higher mortality rate than those subjects not on pressors during the time of the MAX rate, a higher number of types of GI intolerance symptoms per subject (stool output >1L per day, GRV >500 mL, aspiration, necrotic bowel), and a significantly higher incidence of necrotic bowel after the MAX rate (Table 3).

Promotility agents were used either before or during the MAX rate in 33% of the subjects. Being on a promotility agent at the start of the MAX rate was not associated with any negative outcomes, nor did it result in a significant difference in GI tolerance (Tables 4, 5). Subjects who had a promotility agent added after initiation of the MAX rate received the MAX rate for a longer period of time than subjects who did not have a promotility agent added after initiation, significantly higher GRV during the MAX rate, experienced more episodes of emesis and had higher number of types of GI intolerance symptoms per subject. (Table 7).

Table 3

Subjects on Pressor Agents During MAX Rate

Characteristic	Yes (n=22)	No (n=129)	p-value
Total number of GI intolerance symptoms per subject	1.0 (0.0, 2.0)	0.0 (0.0, 1.0)	0.024
Any of these GI intolerance symptoms	15 (69%)	62 (48%)	0.081
Mortality	15 (68%)	30 (23%)	<0.001
MAX[1] rate ordered (mL/hr)	152.3 ± 57.2	149.9±41.1	0.720
Hours at MAX rate	150.0 (41.0, 321.0)	52.0 (16.5, 132.5)	0.009
Post-pyloric feeding prior to MAX rate	9 (43%)	68 (53%)	0.380
Promotility agent added during MAX rate	5 (23%)	12(16%)	0.195
Emesis during MAX rate	4 (18%)	21 (16%)	0.824
Highest GRV[2] during MAX rate (mL)	445.0 (142.5, 525.0)	140.0 (0.0, 340.0)	<0.001
Stool output >1L/day during MAX rate	10 (46%)	42 (33%)	0.239
GRV >500mL during MAX rate	5 (23%)	14 (12%)	0.151
Aspiration during MAX rate	2 (9%)	1 (0.7%)	0.056
Necrotic bowel during MAX rate	0 (0%)	7 (5%)	0.594
Necrotic bowel after MAX rate	7 (32%)	11 (9%)	0.002

Table 3 Definitions: [1] maximum enteral feeding flow rate ordered and received measured in mL/hr, [2]gastric residual volume. *p < 0.05, Data presented as mean ± standard deviation, median (IQR) or n(%)

Table 4

Subjects on a Promotility Agent at the Start of MAX Rate

Characteristic	Yes (n=29)	No (n=122)	p-value
Total number of GI intolerance symptoms per subject	1.0 (0.0, 2.0)	1.0 (0.0, 1.0)	0.447
Any of these GI intolerance symptoms	15 (55%)	61 (50%)	0.384
Mortality	9 (31%)	36 (30%)	0.872
Post-pyloric feeding prior to MAX[1] rate	17 (59%)	60 (50%)	0.404
Emesis during MAX rate	7 (24%)	18 (15%)	0.221
Highest GRV[2] during MAX rate (mL)	200.0 (0.0, 400.0)	160.0 (20.5, 375.0)	0.976
Stool output >1L/day during MAX rate	12 (41%)	40 (33%)	0.381
GRV >500mL during MAX rate	3 (10%)	16 (14%)	0.765
Aspiration during MAX rate	0 (0%)	3 (3%)	1.000
Necrotic bowel during MAX rate	2 (7%)	5 (4%)	0.619
Necrotic bowel during or after MAX rate	4 (14%)	14 (12%)	0.751

Table 4 Definitions: [1] maximum enteral feeding flow rate ordered and received measured in mL/hr, [2]gastric residual volume. *p < 0.05, Data presented as median (IQR) or n(%)

Table 5

Subjects with Promotility Agent Added during the MAX Rate

Characteristic	Yes (n=21)	No (n=130)	p-value
MAX rate ordered[1]	146.5 ± 36.9	150.9 ± 44.7	0.802
Hrs subject received MAX rate	111.0 (74.0, 233.5)	47.0 (14.0, 149.8)	0.002
Mortality	5 (24%)	40 (31%)	0.518
Post-pyloric feeding prior to MAX rate	14 (67%)	63 (49%)	0.138
Emesis during MAX rate	7 (33%)	18 (14%)	0.039
Highest GRV[2] during MAX rate (mL)	355.0 (157.5, 530.0)	140.0 (2.5, 350.0)	0.002
Stool output >1L/day during MAX rate	11 (52%)	41 (32%)	0.062
GRV >500mL during MAX rate	5 (25%)	14 (11%)	0.093
Aspiration during MAX rate	1 (5%)	2 (2%)	0.329
Necrotic bowel during MAX rate	0 (0%)	7 (5%)	0.276
Necrotic bowel during or after MAX rate	3 (14%)	15 (12%)	0.718

Table 5 Definitions: [1] maximum enteral feeding flow rate ordered and received measured in mL/hr, [2]gastric residual volume. *$p < 0.05$, Data presented as mean ± standard deviation, median (IQR) or n(%)

Subjects in Table 6 who had any GI intolerance symptoms (GRV over 500 mL, aspiration, necrotic bowel, emesis, stool output >1L in 24 hrs) had a higher MAX rate, were on the MAX rate for a longer period of time, were significantly older, had a higher % TBSA burn, and had a higher REE than those subjects who did not have any GI intolerance symptoms while on the MAX rate.

Subjects who experienced emesis during the MAX rate were younger and had a significantly higher % TBSA burn, higher REE, higher MAX rate, received the MAX rate over a longer period of time, had higher stool volume outputs, higher maximum GRV's, higher incidence of residuals >500 mL, higher incidence of necrotic bowel during or after the MAX rate, higher incidence of any GI intolerance symptoms, and higher number of GI intolerance symptoms per subject than subjects who did not experience emesis (Table 7).

Table 6

Any GI Intolerance Symptoms

Characteristic	Yes (n=77)	No (n=74)	p-value
Age, years	39.9 ± 12.6	35.4 ± 15.0	<0.010
Height, inches	69.7 ± 2.5	69.4 ± 3.6	0.618
Pre-injury weight, kilograms	81.4 ± 11.6	83.2 ± 18.8	0.708
%TBSA[1] burn	52.5% ± 18.0%	44.0 % ± 16.3%	0.002
Predicted REE[2]	2801.1 ± 506.2	2534.4 ± 509.0	0.001
MAX[3] rate ordered (mL/hr)	156.6 ± 38.8	143.7 ± 47.5	0.027
Hours subject received MAX rate	105.0 (45, 232)	29.5 (12, 73.4)	<0.001
Post-pyloric feeding prior to MAX rate	40 (53%)	37 (50%)	0.683
Mortality	26 (34%)	26 (19%)	0.277

Table 6 Definitions: [1]percent total body surface area burned, [2]resting energy expenditure, [3] maximum enteral feeding flow rate ordered and received measured in mL/hr. Data presented as mean ± standard deviation, median (IQR) or n(%)

Table 7

Subject Experienced Emesis During the MAX Rate

Characteristic	Yes (n=77)	No (n=74)	p-value
Mortality	26 (34%)	19 (26%)	0.277
Age, years	26.8 ± 6.1	33.7 ± 14.9	0.010
Height, inches	70.0 ± 2.9	69.5 ± 3.2	0.618
Pre-injury weight, kilograms	80.4 ± 10.1	82.7 ± 16.5	0.709
%TBSA[1] burn	54.3 ± 17.3	47.2 ± 17.6	0.002
Predicted REE[2] (kcal/day)	2887.4 ± 461.0	2626.0 ± 525.8	0.002
MAX[3] rate ordered (mL/hr)	161.2 ± 22.9	148.1 ± 46.4	0.027
Hours at MAX rate	217.0 (60.0, 408.0)	47.0 (14.0, 116.5)	<0.001
Post-pyloric feeding prior to MAX rate	40 (53%)	37 (50%)	0.684
Highest GRV[4] during MAX rate (mL)	250.0 (70.0, 447.5)	150.0 (10.0, 367.5)	<0.001
Stool output >1L/day during MAX rate	52 (68%)	0 (0%)	<0.001
GRV >500mL during MAX rate	19 (26%)	0 (0%)	<0.001
Aspiration during MAX rate	3 (4%)	0 (0%)	0.245
Necrotic bowel during MAX rate	7 (9%)	0 (0%)	0.014
Necrotic bowel during or after MAX rate	18 (23%)	0 (0%)	<0.001

Table 7 Definitions: [1]percent total body surface area burned, [2]resting energy expenditure, [3] maximum enteral feeding flow rate ordered and received measured in mL/hr, [4]gastric residual volume. Data presented as mean ± standard deviation, median (IQR) or n(%)

There was not a strong association between predicted REE, pre-injury weight, age, hours subjects received MAX, % TBSA burn and the highest GRV during the MAX rate (Table 8). There was not a strong association between highest GRV during MAX, pre-injury weight, age, hours subject received MAX, % TBSA burn, and total number of GI intolerance symptoms (Table 8).

Subjects who had GRV greater than 500 mL during the MAX rate received the MAX rate for a longer time period than subjects without GRV greater than 500 mL (Table 9). Two of the three subjects in the study who aspirated during the MAX rate also had GRV greater than 500 mL per day.

There were three subjects in this study who aspirated, none of which survived (Table 10). These subjects were male and two of the three had necrotic bowel during or after the MAX rate. All three of the subjects had a high stool volume output; however, none of the subjects experienced emesis. None of these three subjects were on a promotility agent at the initiation of the MAX rate. Two of the three subjects who aspirated were also on pressors at the time of MAX rate.

Table 8

Linear Regression of Highest GRV During the Max Rate

Highest GRV During the Max Rate	R^2 Value
vs. Predicted ISR REE	0.028
vs. Pre-injury weight	0.007
vs. Age	0.002
vs. Hours Subjects Received MAX rate	0.032
vs. % TBSA burned	0.007

Table 10

Table 9

Subjects Aspirated During the MAX Rate

Characteristic	Yes (n=3)	No (n=147)	p-value
Mortality	3 (100%)	42 (29%)	0.025
Age, years	48.0 ± 32.9	32.1 ± 13.4	0.350
Height, inches	67.7 ± 3.5	69.6 ± 3.1	0.293
Pre-injury weight, kilograms	75.7 ± 16.1	82.4 ± 15.7	0.590
TBSA[1] burn	47.1 ± 17.5 %	28.3 ± 17.6	0.568
Predicted REE[2] (kcal/day)	2549.7 ± 815.5	2681.9 ± 516.1	0.372
MAX[3] rate ordered (mL/hr)	101 ± 38.2	88.5 ± 43.7	0.239
Hours at MAX rate	155.0 (154.1, 181.0)	60.1 (15.4, 153.0)	0.677
Post-pyloric feeding prior to MAX rate	1 (33%)	76 (52%)	1.000
Highest GRV[4] during MAX rate (mL)	520.0 (100.0, 800.0)	52.0 (16.5, 142.5)	0.141
Pre-pyloric feeding prior to MAX rate	1 (33%)	63 (43%)	1.000
Aspiration during MAX	2 (67%)	9 (6%)	0.134
Aspiration bowel during or after MAX rate	2 (67%)	1 (1%)	0.038
Necrotic bowel during MAX rate	1 (33%)	5 (3%)	0.579
Necrotic bowel during or after MAX rate	1 (33%)	12 (8%)	0.229

Table 9 Definitions, [1]percent total body surface area burned, [2]resting energy expenditure, [3]maximum enteral feeding flow rate ordered and received measured in mL/hr, [4]gastric residual volume. Data presented as mean ± standard deviation, median (IQR) or n(%)

GRV >500mL During the MAX Rate

Characteristic	Yes (n=19)	No (n=125)	p-value
Mortality	8 (42%)	36 (29%)	0.240
Age, years	37.7 ± 18.1	32.8 ± 13.9	0.574
Height, inches	69.1 ± 3.4	69.6 ± 3.1	0.961
TBSA burn	41.1 ± 17.5 %	28.8 ± 17.6	0.577
Pre-injury weight, kilograms	83.5 ± 15.5	82.2 ± 16.1	0.551
Predicted REE (kcal/day)	2706.6 ± 614.1	2668.1 ± 512.5	0.431
MAX rate ordered (mL/hr)	121 ± 38.2	87 ± 43.7	0.240
Hours at MAX rate	120.0 (100.0, 180.0)	60.0 (15.0, 137.5)	0.001
Post-pyloric feeding prior to MAX rate	12 (67%)	63 (51%)	0.196
Aspiration during MAX	2 (11%)	1 (1%)	0.047
Aspiration bowel during or after MAX rate	2 (11%)	1 (1%)	0.047
Necrotic bowel during MAX rate	1 (5%)	5 (4%)	0.579
Necrotic bowel during or after MAX rate	4 (21%)	12 (10%)	0.229

Table 10 Definitions, [1]percent total body surface area burned, [2]resting energy expenditure, [3]maximum enteral feeding flow rate ordered and received measured in mL/hr. Data presented as mean ± standard deviation, median (IQR) or n(%)

Subjects who had high stool volume output (>1L in 24 hrs) during the MAX rate had a significantly higher % TBSA burn, higher maximum GRV's, more occurrences of aspiration, and received the MAX rate for a longer time period than subjects with stool volume outputs <1L per day (Table 11). Subjects who had stool output >1L/day during MAX had an average of 52.7 ± 18.5 % TBSA (p= 0.034), an average MAX rate of 157.6 ± 37.7mL/hr (p=0.127), and GRV >500mL/day (p= 0.028) compared to subjects who did not have stool output >1L per day during the MAX rate.

There were seven subjects who had necrotic bowel during the MAX rate (Table 12). All seven subjects were male. None of the subjects were on pressors or experienced emesis during the MAX rate. These seven subjects were on the MAX rate for a shorter duration of time than those subjects who did not have necrotic bowel. Subjects who had necrotic bowel during the MAX rate had a higher mortality. There were 18 subjects who had necrotic bowel during or after the MAX rate (Table 13). These subjects had a higher TBSA burn and REE. The subjects who had necrotic bowel had a significantly higher mortality rate than subjects who did not have necrotic bowel.

Table 11

Stool output >1L per day during the MAX rate

Characteristic	Yes (n=52)	No (n=99)	p-value
Mortality	18 (35%)	27 (27%)	0.349
Age, years	30.6± 13.8	33.6 ± 14.2	0.080
Height, inches	69.5 ± 2.6	69.6 ± 3.4	0.787
Pre-injury weight, kilograms	81.2 ±12.2	82.9 ± 17.2	0.626
%TBSA[1] burn	52.7 ± 18.5	46.1±16.9	0.034
Predicted REE[2] (kcal/day)	2778.8 ± 523.1	2611.5 ± 516.7	0.065
MAX[3] rate ordered (mL/hr)	157.6 ± 37.7	146.4±46.1	0.127
Hours at MAX rate	118.0 (58.8, 249.3)	34.0 (12.0,97.0)	<0.001
GRV >500mL during MAX	11 (22%)	8 (9%)	0.028
Post-pyloric feeding prior to MAX rate	28 (56%)	49 (50%)	0.453
Aspiration during MAX	3 (6%)	0 (0%)	0.040
Necrotic bowel during MAX rate	2 (4%)	5 (5%)	1.000
Necrotic bowel during or after MAX rate	9 (17%)	9 (9%)	0.148

Table 11 Definitions: [1]percent total body surface area burned, [2]resting energy expenditure, [3] maximum enteral feeding flow rate ordered and received measured in mL/hr. Data presented as mean ± standard deviation, median (IQR) or n(%)

Table 12

Necrotic Bowel During the MAX Rate

Characteristic	Yes (n=7)	No (n=144)	p-value
Mortality	5 (71%)	40 (28%)	0.030
Age, years	24.9 ± 5.5	32.9 ± 14.3	0.126
Height, inches	69.8 ± 2.0	69.6 ±3.2	0.835
Pre-injury weight, kilograms	72.7 ± 6.0	82.5 ± 15.7	0.184
%TBSA[1] burn	54.4 ± 20.4	48.0 ± 17.5	0.360
Predicted REE[2] (kcal/day)	2842.0 ± 645.0	2662.3 ± 519.1	0.536
MAX[3] rate ordered (mL/hr)	159.3 ± 52.2	149.8 ± 43.3	0.790
Hours at MAX rate	13.0 (5.0, 20.0)	62.5 (20.0, 162.0)	0.099
Post-pyloric feeding prior to MAX rate	4 (57%)	73 (51%)	1.000

Table 12 Definitions: [1]percent total body surface area burned, [2]resting energy expenditure, [3] maximum enteral feeding flow rate ordered and received measured in mL/hr. Data presented as mean ± standard deviation, median (IQR) or n(%)

Table 13

Necrotic bowel during or after the MAX rate

Characteristic	Yes (n=18)	No (n=131)	p-value
Mortality	14 (78%)	31 (23%)	<0.001
Age, years	28.9±10.6	33.1 ± 14.5	0.241
Height, inches	69.2 ±3.1	69.6 ± 3.1	0.794
Pre-injury weight, kilograms	82.3 ± 14.1	82.3 ± 15.8	0.991
%TBSA[1] burn	57.0 ± 20.0	47.1% ± 17.1	0.047
Predicted REE[2] (kcal/day)	2919.3 ± 479.5	2637.6 ± 521.7	0.036
MAX[3] rate ordered (mL/hr)	157.8 ± 41.8	149.2 ± 43.9	0.394
Hours at MAX rate	17.0 (8.8, 136.0)	62.0 (20.5, 159.0)	0.130
Post-pyloric feeding prior to MAX rate	7 (39%)	70 (53%)	0.246

Table 13 Definitions: [1]percent total body surface area burned, [2]resting energy expenditure, [3] maximum enteral feeding flow rate ordered and received measured in mL/hr. Data presented as mean ± standard deviation, median (IQR) or n(%)

Chapter 5: Discussion and Conclusion

There was no MAX rate threshold found when MAX rates in subjects with severe burns were evaluated against emesis, aspiration, elevated stool output, elevated GRV's, necrotic bowel, and survival.

There is not a consensus on a MAX rate in an adult burn patient population. This is due to the lack of research available on this specific topic. Secondary findings of this study included predictors of mortality based on age, burn size, and total number of GI intolerance symptoms.

This study confirmed several findings already known to be true in current research. Age and large burn size were found to be positive predictors of mortality ($p < 0.0001$). Survivors had 44 ± 15% TBSA burn, and those who died had 58 ± 20% TBSA ($p = <0.01$). For every one year increment increase in age, the subject's mortality odds increased by 7% and for every 1% increase in burn size, mortality odds increased by 8% (Table 2). This is similar to previous reported data. [41] Muller, et al. found that burn size was the strongest independent variable in predicting mortality ($p = <0.001$). A burn size of 35% TBSA burn had a 95.5% increased risk of mortality when compared to a burn size of 2% TBSA. [41]

Age was the second strongest independent variable to predict mortality in this study. Subjects who were 48 years of age have previously been found to have a mortality rate 7.3 times higher than that of a 20 year old. [41] In another study, the most significant variables contributing to mortality were >40% TBSA burn, >60 years of age, and inhalation injury, with an average increase of 3% for one risk factor, 33% for two risk factors, and 87% for three risk factors. [11]

The total number of GI intolerance symptoms the individual subject experienced during MAX rate also predicted mortality in this study ($p = 0.011$). For each additional GI intolerance symptom a subject experienced, their mortality odds increased by two fold (Table 2). Survivors

experienced an average of 0.7 ± 0.8 types of GI intolerance symptoms during MAX rate, whereas those subjects who died experienced 1.0 ± 1.1 types of GI intolerance symptoms during MAX rate (p=0.16). This predictor of mortality has not been found, but GI intolerance has been linked to sepsis in burn patients. [42]

Gungabissoon, et al. examined the impact of enteral feeding intolerance on clinical outcomes in an ICU population. Enteral feeding intolerance was defined as one or all of the following symptoms: emesis, diarrhea, abdominal distention, GRV > 200mL, or subject complaint of abdominal discomfort. [29] It was found that subjects flagged for feeding intolerances were alike in age, BMI, gender, and acuity of illness in comparison to subjects who had no reported feeding intolerances. [29] Gungabissoon found that subjects who tolerated their enteral feeds had shorter ICU stays and more ventilator-free days. [29]

Subjects with higher maximal enteral rates were noted to have more episodes of emesis, (p=0.02). Subjects in this study who were reported to have emesis during the MAX also had a higher incidence of the following: necrotic bowel before and after the MAX (p <0.001), GRV >500mL (p<0.001), and stool output >1L in 24 hrs (p <0.001). Another study examined GRV as a marker for enteral nutrition intolerance by comparing three groups of subjects receiving total enteral nutrition with nasogastric tube placement in the stomach. The three groups analyzed included 10 ICU subjects, 8 stable patients from a medicine ward, and a comparison group of 20 healthy volunteers. (McClave, 1999). McClave's study required subjects to remain in bed and receive an uninterrupted continuous feed for eight hours. Intolerance was diagnosed with both a physical exam and radiologic confirmation. Enteral feeding rates were determined on an individual basis so that all subjects received 25 kcal per kilogram with an average flow rate of 92.5mL/hr. Results showed that enteral infusion rates were directly proportional to GRV's.

McClave concluded that for enteral feeding to the stomach, residual volumes >200mL may be an indicator of delayed gastric emptying and increase a patient's risk for emesis and aspiration. [30]

It is difficult to determine the etiology of diarrhea in tube fed patients as the cause can be multifactorial including infection, medication, and enteral feeding formula selection or infusion rate. The incidence and etiology of diarrhea in tube fed burn patients has been examined in current research and found that half of the confirmed reports of diarrhea were related to antibiotic administration ($p < 0.005$). [17] It is noted that these subjects had an average of 45% TBSA burn. Other significant etiologies included dietary lipid content of the enteral formula ($p < 0.05$) and vitamin A intake ($p < 0.001$). [17] Gottschlich et. al., found using a low-fat, vitamin A-enriched hypotonic modular formula to be the best treatment for diarrhea related to enteral feedings ($P < 0.00001$).

Subjects who experienced necrotic bowel during or after the MAX had a high mortality rate ($p=<0.001$) and greater than 50% TBSA burn ($p=0.047$). The MAX rate was not significantly different in those subjects with necrotic bowel during or after the MAX compared to subjects without necrotic bowel during or after the MAX. Necrotic bowel was a frequent complication noted in burned patients admitted to the USAISR from 2003-2008 (n=31) with a mortality rate of 68% in these subjects.[43] They examined all burn subjects with abdominal complications admitted during this time, regardless of if they received EN. We examined only the subjects with at least 20% TBSA burn who were receiving EN and found a mortality rate of 78% in those with necrotic bowel diagnosed during or after the MAX rate the subjects received. Markell also found no significant association with EN provision and necrotic bowel.[43]

Increased duration of enteral nutrition and improved clinical outcomes was a secondary finding of this study consistent with current research findings. Subjects who received the MAX

rate for a longer duration of time had a lower incidence of any GI intolerance ($p<0.001$) (see Table 4). This finding is consistent with early initiation of enteral nutrition in a burn patient population as described by Moiser, et al. [22] According to Moiser, early enteral nutrition was defined as initiation within the first 24 hours of admission. Moiser and colleagues confirmed that early enteral nutrition gave a burned individual a shorter ICU stay, lower incidence of burn wound infections, ileus, and stress ulceration.

Hart, et al confirmed that improved outcomes in protein catabolism and wound healing in burned patients occurred with continued aggressive enteral feeding. [20] ICU's implementing the PEP uP Protocol had less gastrointestinal complications, lower ICU mortality rates, more ventilator free days, and shorter hospital stays. [28] These patients also received 60.1±29.3% of prescribed calories from EN ($p =0.02$) and 61.0 ± 29.7% of prescribed protein from EN ($p=0.01$).[28]

Although a standard for a MAX rate could not be established, this study provoked additional clinical practice questions based on our findings. This study did not explore whether or not the addition of a promotility agent reduced GRV's or emesis during MAX. It may be beneficial in the future to explore the timing of initiating a promotility agent with increasing enteral rates to provide standards for clinical practice.

There was a strong association between emesis and additional negative outcomes, although this is not necessarily causal (Table 7). Further research is needed to determine whether or not emesis is a true predictor for additional negative GI outcomes.

The strengths of the study were a large number of subjects and it is currently the only study on this topic. Another strength is that we examined a period of time with increased necrotic bowel. This is a difficult problem to study, as it is a rare occurrence.

The greatest limitation of the study was the retrospective design. Due to the retrospective study design these additional factors and their possible effects on the tolerance of EN were not analyzed: additional medical complications post-operatively, blood pressure medications that may affect GI motility or contribute to large stool volume, mechanical ventilation or intubation, clostridium difficile, sepsis, mucormycosis, and additional systemic infections.

Since this study was conducted at a military burn unit during the height of the Iraq War in the early 2000's, factors such as blast injuries, amputations, and poly-trauma could impact mortality. These additional factors were not taken into consideration or measured as part of this study but would be variables to consider in future studies.

Women were a small portion of the subjects studied following a consistent pattern for gender of burn patients in other studies [11] and annual data provided by the National Burn Repository. [44] The high military rate (69%) may make the data less applicable to civilian burn centers, as the military burn patient population has been found to have less pre-existing conditions than the civilian burn population.[45] The cause of the higher mortality rate in those subjects on pressors is likely multifactorial and not unexpected. [11]

Conclusion

This population of severely burned subjects (48.3% ± 17.6% TBSA) received an average MAX rate of 153.6 ± 45.2 mL/hr. The MAX rate was not a significant cofounder in predicting mortality; however, age, burn size, and the number of types of GI intolerance symptoms the individual subject experienced during MAX rate were predictors for mortality ($p = 0.011$). There was a significantly higher mortality rate and a significantly higher number of types of GI intolerance symptoms experienced per subject during MAX rate associated with subjects receiving pressors during the MAX rate ($p = <0.001$).

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