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13. SUPPLEMENTARY NOTES

14. ABSTRACT - Our Study/Product Aim(s) were as follows: 1) To determine compliance with nutritional goals in severely burned adults, 2) To find strategies to address identified gaps in feeding, and 3) To develop and test a system that incorporates the above strategies. The proposed system would provide points in a checklist for provider attention and decision support guidelines to meet nutritional goals. For the project. we expended significant effort in obtaining approval, auditing, and analyzing data from several hundred severely burned subjects treated in the ICU from 3 centers. The current analysis using data collected without DoD funds, but the approval process, auditing of the data, and analysis was all done with time allocated to the grant, showed that initiation of tube feedings was within the first 24 hours in the majority, but the patients underwent 3±3 operative procedures and in 53% of the hospital days tube feedings were held for clinical reasons, and restarted with only a minor effort to increase feedings to meet nutritional recommendations. Further, we found on average that patients received below the average daily caloric intake for normal persons despite increased needs associated with injury and hypermetabolism. This was associated with significant weight loss and hypoalbuminaemia. These data demonstrate that a decision support system to meet nutritional recommendations is clearly needed that could be done with a decision-support software package. The SOW was not completed as the PI has moved to another institution. Work will continue without the use of DoD funds to complete the goals of the project.

15. SUBJECT TERMS
Severe burns, nutritional support, decision support

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INTRODUCTION

We began this project with a goal to define the modern practice of nutritional provision in burn units in the United States, including the severely burned combat casualty. With this data, we intended to analyze it using control theory techniques to determine how and when deficits in recommended nutrition provision occurred, and devise a decision-support tool to provide real-time recommendations to providers such that the severely burned patient would be more likely to meet nutritional recommendations. We devised this project in response to a Program Announcement from the Department of Defense in 2012 that was soliciting proposals for developing for development and testing of checklists with burn care in the Intensive Care Unit. The proposal to address the goals above was submitted using techniques we developed with decision support technology in burn resuscitation. To perform this project, we initially assembled investigators from 4 Texas burn centers to submit data on nutritional provision in the burn ICU. As stated above, we intended to use these data to analyze for gaps in nutritional provision and how these could be met using recommendations provided with decision support technology. The technology was proposed to be computer based and real-time. We devised the following overall hypothesis: **A computerized checklist for the Burn Intensive Care Unit (BICU) that provides guidelines and information on current and cumulative nutritional provision *and* decision support for subsequent nutritional orders improves compliance with nutritional goals.** We proposed to test this hypothesis through addressing the following *Specific Aims*:

- To determine under what conditions compliance with nutritional goals are not met in severely burned adults.

We sought to collect retrospectively nutritional data submitted to the medical record in four burn centers to assess nutritional provision in relation to local nutritional goals with identification of periods of upward and downward variances from hourly goals. We then planned to correlate these identified deficits and excesses to clinical events and objectively define the incidence and timing of gaps in feeding and times above goals. From this analysis, we would identify targets for improvement.

- To find strategies to address identified gaps in feeding.

With the analysis described above, we expected to find gaps during the initiation of feeding, gaps during and following expeditions from the ICU for clinical tests and procedures, and gaps in actions from providers who ordered decreases or termination of enteral feeding during perceived periods of higher risk, such as during periods of high gastric residuals or systemic hypotension. The analysis was designed to also determine other gaps that were unexpected. With this data, we proposed to model and report the practice of nutritional provision in the modern BICU that fully identifies gaps and excesses in relation to local recommendations. With this information, we could devise safe strategies to meet recommended nutritional provision, and determine safe times to temporarily increase feeding rate to close measured gaps; these times would be identified with a decision-support tool and would provide recommendations for rectification.

Once these two aims were met, the information was proposed to construct a nutritional decision support checklist using the developed model and a computerized decision support system to display current information including current feeding rate, daily totals, and hospital stay cumulative totals. This would then be aligned with daily and cumulative goals to serve as a traditional checklist for nutritional provision. Then, the model devised from the data collected would provide hourly recommendations to the feeding rate to meet recommended goals. Thus, the third aim of the project:

- To develop and test a system that incorporates the above strategies. The system would provide points in a computerized checklist for intermittent provider attention *and* decision support guidelines for appropriate changes to meet cumulative and current nutritional goals.

These aims are encapsulated in the following revised *Statement of Work*:

Background: Activity in the burn intensive care unit (BICU) is complex, variable, and can be difficult to coordinate towards the overall goal to improve outcomes. Relatively new technologies are available to assist providers with monitoring critical care activities to be aware of physiologic and treatment changes as well as provide recommendations meet these changes to reach desired goals. One such area in the Burn Intensive Care Unit is in the area of nutrition; providers are in universal agreement to the advisability of feeding to meet nutritional goals, but in spite of this, only 70-80% of goals are typically met. This is thought to be due to temporary interruptions to decrease the risk of complications or to meet other goals. Further, providers are often unaware of accumulating deficits over the hospitalization, and if recognized need safe and effective strategies to temporarily accelerate feeding to meet goals.

Objective: To develop and implement a checklist with a decision support system to inform BICU providers of nutritional provision in relation to goals and provide a safe strategy to meet desired nutritional provision.

Project Breakdown:
TASK ONE: After award of funding, we will seek IRB and HRPO approval then proceed with data collection of hourly nutritional delivery and associated feedback variables until enrollment goals are reached at 3 study centers (University of Texas – Southwestern Medical Center, the University of Texas Medical Branch, and the University of Texas Health Science Center – Houston). This will consist of two separate sets of data: the first will be from data that were already obtained by the investigators at the three centers. The second set will come from adding 200 additional subjects to the already obtained data to extend the findings, which will also come from all three centers. Approval to collect and analyze the data from HRPO will be sought independently for each data set, the existing data (set 1), and new data (set 2). These data will then audited for reliability and reproducibility.
TASK TWO: Once the data are codified, these will be used to develop a physiologic model of feeding and associated responses across time in severely burned patients. From this model, a checklist and decision support system will be constructed to give providers a real-time assessment of progress towards nutritional goals as well as recommendations for changes in feeding based on model predictions to reach and maintain goals.
TASK THREE: Once constructed, the Burn Nutrition and Decision Support System (BNS) will be tested for reliability in a crossover design to assess feasibility, reliability, safety, and efficacy. The final product will then be available for patent and FDA testing.

KEYWORDS

Nutrition, severe burn, decision support

OVERALL PROJECT SUMMARY

As of March 2018, the Principal Investigator has left the Institution and the scope of work has remained incomplete. UT Southwestern has asked for early termination of this award. Any continuance of this project will be done without Department of Defense funds.

TASK ONE: We received IRB approval for collection of data at University of Texas – Southwestern Medical Center, University of Texas Health Science Center – Houston, the University of Texas Medical Branch in Galveston, and then we completed collection of 100 subjects at UT-Southwestern, 42 at the University of Texas Health Science Center – Houston, and 100 at the University of Texas Medical Branch in Galveston. These data served as the first analysis and were included in the abstracts listed below. The data analysis done at that time at the three centers are summarized with the following:

Median age was 41 [25,56], TBSA burned 37% [24,55], full thickness burn area 20% [8,43], 31% had inhalation injury. Admission weights were 79 kg [66,94], and discharge weights 70 kg [63,81]. Average weight loss during the hospitalization was 7 kg [-15,-2] and percentage loss from admission weight was 9% [-17,-3]. Tube feedings were started on the day of admission in 43%, and within one day of admission in 78%; < 12% were started more than 48 hours from admission. Duration of tube feedings was 18 days [10,30] for this population; ICU days with tube feedings given was 91% [64,100], and for the whole hospitalization was 67% [44,91].

Of note, the collection of these data was done after site IRB approval at the University of Texas – Southwestern Medical Center, the University of Texas Medical Branch, and the University of Texas Health Science Center – Houston for the research. We were unable to gain full participation from the United States Army Institute of Surgical Research at the outset of the grant, and worked side-by-side with them in development of a product. They reported a budgetary adjustment for an independent assessment was made within the Department of Defense, and thus they chose to participate in development of the product but not in data collection or analysis. Therefore, we continued with the project in full at the three centers listed above utilizing non department of defense funds.

At this point, we encountered some administrative and regulatory hurdles. Since the data collection was retrospective and no more than minimal risk, we were unaware that a second-level of review and approval by the Human Research Protections Office (HRPO) of the Department of Defense was required for this low level of investigation, as any potential benefits and risks to research subjects of other ethical issues had been addressed according to the Belmont Report and 45CFR46 by the local Institutional Review Boards, all with Federal Certificates of Assurance. The project was halted for a significant period of time after we became aware of this regulation, and hundreds of hours of work were expended by the Principal Investigator and his staff to rectify these efforts and meet regulatory approval for use of the collected data, which took more than one year of effort. Adjustments were made to the budget and Statement of Work with the agreement to continue the project using the data that had been independently collected as well as further data collection to enhance the findings. This was approved by the Grants Office Representative and the Contracting Office Representative. The data collection effort itself was not allocated to the grant and DoD funds, but all analysis of the data after approval was assigned to the project, which was also hundreds of hours of work. This as well as securing regulatory approval accounted for almost all the effort expended and accounted to the grant.

In the period of funding, we also expended significant effort with hundreds of hours of work in negotiating and preparing documents for the agreed upon second data collection with additional local IRB approval and HRPO approval at the study sites for this no more than minimal risk retrospective study; these efforts ceased once we elected to close the project in February 2018. We have also spent many weeks and months of effort in preparing reports. During this period, no Department of Defense grant funds were allocated or spent.

Once HRPO approval was secured for the Parkland data, we reformatted and analyzed the data in hand, which is summarized with the following:

In this cohort, the average was 43 ± 22 (SD), and median age was 46 [26, 56] (IQR). Average burn size was 34 ± 23 % TBSA, and median 31 % TBSA [15, 45]; full thickness burns were average 21 ± 20% TBSA and median 18 % TBSA [7, 30]. Twenty percent were diagnosed with inhalation injury, and mortality was 11%. The demographics of ALL consecutively patients receiving enteral feedings at this site by tube in the prescribed period of the study suggest that this is a severely burned population that is likely to benefit from nutritional provision. Thus, this treatment is likely to be appropriate and should be maximized.

Of interest, this population underwent an average of 3 ± 3 (SD) operative procedures (median 2 [1, 3]) during the hospital stay; each of these warrants holding feedings and necessarily induce variability in the tube feeding rate. Additionally, approximately one operative procedure for each 15% TBSA was incurred. This suggests that a checklist and decision support tool to control rates at the recommended volumes would be of clear benefit, and thus support the goals of the project. Additional information from the analysis note an average of 37 ± 29 days in the hospital (median 29 [20, 50]), or indexed to burn size at 1.7 ± 2.5 days/% TBSA burned (median 1.1 [0.7, 2.0]) which provides further support.

For the nutritional provision, the recommended delivery assigned by the treatment team for the population was 2122 ± 619 kcal/day, which is clearly achievable. The routine intake of an adult in the United States is currently 2195 kcal/day. However, our initial analysis revealed that for the days in the hospital receiving enteral feeding, only 75 ± 16% of the recommended caloric delivery was met. We found that on average the patients above received enteral tube feeding an average of 23 ± 26 days (median 29 [20, 50], indicating that patients are generally underfed when receiving tube feedings. Further, we found that an average of 12 ± 12 days of the 23 (53 ± 21% of tube feeding days) had a significant hold on feeding for clinical events. These changes correlated with an average deficit in caloric delivery/day of 441 ± 320 (median 360 [254, 519]). We also found the number of days that calories were achieved that were above recommended volumes was only 1 ± 1 days of hospitalization (median 0 [0, 1]) suggesting that little effort was made to make-up deficits. These data indicate a clear deficit in the provision of recommended caloric delivery in severely burned patients who are being tube fed. Further, the deficits are continued and prolonged for weeks in some cases. This suggests that corrections should be made perhaps using computer and decision support technologies.

Finally, the clinical outcomes in this population is as follows. Serum albumin was tracked as a nutritional marker, and the average nadir in this value was 1.9 ± 0.6 g/dl (median 1.8 [1.4, 2.1]). The normal range is 3.5-5.0 g/dl, indicating some nutritional deficiency as well. Weight loss averaged 4.4 ± 12 kg (median 3.2 [2, 11]).

In this cohort, 11 children were included. When these were excluded to be more in accord with combat casualties, the average age was 47 ± 18 (median 49 [33, 58]). Burn size was 34 ± 23 % TBSA (median 31 [14, 45]); full-thickness 21 ± 19 % TBSA (median 18 [7, 30]). Twenty-two percent had inhalation injury, and mortality remained at 11%. Operative procedures also remained at 3 ± 3 per patient at about one per 15% TBSA. Hospital stay increased to 38 ± 29 days (median 30 [20, 50]); indexed to burn size this was 1.9 ± 2.6 days/% TBSA (median 1.2 [0.7, 2.1]). When deaths were excluded, this was increased to 2.0 ± 2.8 days/% TBSA (median 1.2 [0.8, 2.3]). Recommended caloric delivery increased to 2202 ± 568 kcal/day, which is still in line with normal caloric intake, and 77% of this was given during the period of tube feeding which was over 24 ± 26 days (median 18 [8, 33]). Caloric deficit was 442 ± 303 kcal/day (median 357 [261, 505]) which was somewhat tighter in this group, suggesting that the deficit was more in accord with normal and established treatment. However, this is far below the recommended caloric delivery suggesting that a checklist and decision-support tool for each patient would be of benefit.

The above analysis confirms that nutritional deficits in the severely burned are common and prolonged. This analysis is currently being bolstered by data from the other centers and will be included in the manuscript under preparation, Nutrition in modern burn centers. It will also be formulated into an abstract for presentation at an upcoming national meeting.

At this point, the decision was made to close grant activities by the Principal Investigator as he has moved to a new institution (UTMB) with a new much larger role and set of responsibilities and would have difficulty meeting regulatory guidelines for reporting. Thus, we are not seeking to transfer or continue the award, and we are closing grant activities. All grant expenditures were used for effort in study initiation, data analysis, preliminary efforts at building a product, data reporting, and efforts at regulatory approval for collection of more data with which to formulate the model as described above and below. Going forward, we will continue to use the data and analysis obtained within the project with other funds, and the grant will continue to be acknowledged with any of this work which we hope to leverage and complete the original proposal.

Thus, what was completed in Aim 1 was analysis of the data and validation as described above, and reports given at national meetings described below. We also sought and obtained local approval for more data collection at the University of Texas – Southwestern Medical Center and were in the process of obtaining approval for this work from HRPO. To date, the analysis produced three abstracts which were presented at the Surgical Research Forum locally in Dallas and the American Burn Association Annual Meeting, one review article, and three manuscripts is in revision or preparation. Please see the abstracts and manuscripts at the end of the report. In addition, portions of these data were presented at numerous invited lectures at Grand Rounds presentations (over 5), and national and international invited lectures regarding topics of nutrition and/or the use of decision support technologies (over 10).

ABSTRACTS

Bernal E, Wolf SE. Checklist and Decision Support in Nutritional Care for Burned Patients. Surgical Research Forum, UT-Southwestern 2014

Bernal E, Wolf SE. Checklist and Decision Support in Nutritional Care for Burned Patients. American Burn Association Annual Meeting 2015.

Nicole C Benjamin BS, Jong O Lee MD, Jamie M Heffernan RN, Steven E Wolf MD FACS, Oscar E Suman PhD, Ronald P Mlcak PhD, Clark R Andersen MS, David N Herndon MD FACS. Difference between Recommended Calories and Calories Received in Adults with Massive Burns. American Burn Association Annual Meeting 2015.

MANUSCRIPTS IN PROCESS

Nicole C Benjamin BS, Jong O Lee MD, Jamie M Heffernan RN, Steven E Wolf MD FACS, Oscar E Suman PhD, Ronald P Mlcak PhD, Clark R Andersen MS, David N Herndon MD FACS. Difference between Recommended Calories and Calories Received in Adults with Massive Burns (in revision).

Bernal E, Hodgman EI, Todd Huzar MD, David N Herndon, Charles E Wade, Steven E Wolf. Nutrition in modern burn centers (in preparation).

Bernal E, Huzar T, Wade CE, Benjamin NC, Herndon DN, Wolf SE. Checklist and Decision Support in Nutritional Care for Burned Patients (in preparation).

MANUSCRIPTS PUBLISHED

Clark A, Imran J, Madni T, Wolf SE. Nutrition and metabolism in burn patients. Burns and Trauma 2017, 5: 11. PMID 28428966

TASK TWO: We planned to use the data to develop a physiologic model of feeding and analysis of variability in severely burned patients. From this model, we intended to develop a checklist and decision support system to give providers real-time assessments of progress towards feeding goals, and provide recommendations for changes in feeding to meet these goals.

In working with the ISR in the first two years of the grant, we teamed in construction of the software platform upon which we intended the checklist and decision support system to be employed. We created a computer program to serve as a checklist, which assures the performance of efficacious preventative activities by providing reminders, highlights attention to signals of worsening conditions, and provides guidance for the best response. This program contains a computer model for achieving caloric goals with unpredictable amounts of time allotted to provide these goals. This is done by overshooting the caloric goal and tapering off if there are no interruptions or increasing further if there are interruptions resulting in a caloric deficit (over the past 24 hours) for which the overshoot model has not already managed.

This initial version of the software contained guidelines included defining elevated gastric residuals as >500 ml or repeating values >300 ml, starting a gastric motility agent when high residuals occur, placing a post-pyloric feeding tube if the gastric motility agent does not resolve the elevated residuals, minimizing interruptions, and running a trophic feeding if an ileus occurs (**Appendix 1)**.

We performed the preliminary analysis and began developing a relationship with the Department of Biomedical Engineering at the University of Maryland to further the project; we were preparing to devise a statement of work and financial arrangements when it was decided to halt the project. We expect that we will continue this relationship and development without federal funding through local resources of the PI which will minimize opportunity costs and regulatory costs. The Department of Defense and this grant will continue to be acknowledged in this work as having played a role in funding of the project. We will continue with the following goals:

SUBTASK 1: Complete clinical data reporting on the assessment of modern nutrition

SUBTASK 2: Complete modeling of feeding delivery in the burn unit, identifying gaps in feeding and opportunities for resolution later in the hospital course.

SUBTASK 3: Complete construction of decision support tool and validate with the current database

TASK THREE: Once constructed, the Burn Nutrition and Decision Support System (BNS) was to be tested for reliability in a crossover design to assess feasibility, reliability, safety, and efficacy. This study will be done using other funds with appropriate acknowledgement of the Department of Defense funding.

KEY RESEARCH ACCOMPLISHMENTS

- Data collection performed not funded through this protocol is completed. However, all data have been analyzed with grant funding for reliability, and found to be accurate. Initial analysis was performed showing the population at risk, nutritional recommendations that were assigned, significant feeding deficits that occurred, and correlated clinical effects. Four abstracts have been presented one manuscript in revision and another in preparation, and another review manuscript has been published. The grant funding received for this effort will be acknowledged in any further publications emanating from this work.
- Initial work on the computer platform was performed (**Appendix 1**), and negotiations with an engineering firm to produce the model were initiated and will continue after the grant is terminated utilizing non Department of Defense external funds.

REPORTABLE OUTCOMES

Identification of estimated nutritional deficits of between 20-30% in modern burn centers, and is associated with significant weight loss. Further, these deficits seem to be institutionalized and thus would be low-hanging targets for checklist and decision-support development. Gaps were identified related to stopping tube feedings for operative and other procedures, and from clinical holds on tube feeding rates for other clinical events. Interestingly, initiation of tube feedings was not a reason for measured nutritional deficits.

Planning for restitution of feeding rate to meet goals with an electronic system is indicated; safety needs should be assessed before instituting such a practice.

CONCLUSIONS

We successfully initiated this study and completed the initial analysis through significant effort which we have presented. Further significant effort was also expended in negotiating other approvals for the retrospective portion at several levels, encountering significant difficulty in maintaining progress due to high opportunity costs. We continued the study with revision of the plan and requests for data analysis and further data collection submitted at the local level. We have also begun construction of the checklist and decision support tool which we expect to complete independently. We will then proceed with clinical testing which will also be done with independent funds.

Checklist and Decision Support in Nutritional Care for Burned Patients

Bernal E, Ross E, Wolf SE

Type of Research: ☐ Basic/Translational or X Clinical

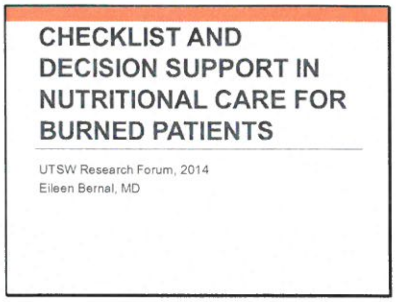
Introduction:
Higher nutritional needs are associated with severe burns, supporting the use of immediate initiation of continuous tube feedings upon admission. However, evidence suggests that only 70-80% of the recommended calories are given. The additive effect of subsequent interruptions and changes in goal rates contribute to the overall failure of reaching 100% of individual goals. Potential causes for delays in initiation include urgent or emergent procedures, while potential causes of interruptions thereafter include expeditions from the ICU or pauses peri-extubation. Dedicated and consistent efforts to compensate for these delays or interruptions are currently lacking. Given that deficits in caloric intake are associated with poor long-term outcomes in severely burned patients, we set out to identify the causes of failure to reach these calculated caloric goals in 100 burned patients admitted to the ICU. After the collection of these data, our aim is to construct a system checklist in which providers can adjust hourly tube feedings real-time to work toward achieving 100% of daily caloric goals.

Methods:
A retrospective chart review of 100 burned patients admitted to the BICU who were initiated on tube feedings was conducted. Data were collected only for the length of first ICU stay per patient. Total hourly volume of tube feedings was recorded for each patient, with the daily goal calculated as the product of hourly goals and total number of hours expected for administration. The difference between tube feedings delivered and the sum of residuals and tube feeds discarded was determined as the actual tube feedings administered. The percentage of expected tube feeding goal was calculated per patent and for the group as a whole.

Results:
The average length of ICU stay was 23.34 days (range 2-189 days) with patients achieving 77.04% ($p<0.01$) of expected goal tube feedings during first ICU stay. Average percent total body surface area and full thickness burn were 34.47% and 21.73%, respectively. Delays in initiation of tube feedings were rare and when present associated with urgent or emergent procedures. Interruptions in continuous tube feedings were attributable to operative intervention in non-intubated patients, trips to MRI, presumed sepsis, high residuals, and pauses peri-extubation attempts. Decreases in daily goal rates were attributable to transition to nocturnal tube feedings and attempts to encourage per os intake. Additionally and where noted, there were certain patient-dictated pauses in continuous tube feedings, due to refusal or noncompliance.

Conclusions:
Severely burned patients have high nutritional needs. Although efforts are made to initiate continuous tube feedings as soon as possible, many burned patients fail to reach their caloric goals. Expeditions from the ICU, pauses for extubation, and high residuals constitute obstacles that interfere with achievement of daily caloric goals. These interruptions can often be anticipated and be compensated for when identified. Given that poor nutritional status is associated with poor long term outcomes, it stands to reason that improvement in nutritional support would promote better outcomes, including the potential for quicker recovery. The information gathered will serve as the foundation for the construction of a system checklist that will enable providers to make more timely adjustments to hourly tube feedings with the overall aim of achieving 100% of expected daily and overall caloric goals. It is the expectation that such a system checklist will help minimize caloric deficits and improve outcomes.

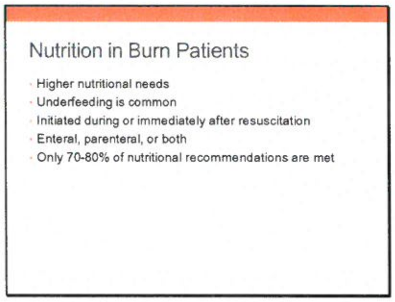
Slide 1



CHECKLIST AND DECISION SUPPORT IN NUTRITIONAL CARE FOR BURNED PATIENTS

UTSW Research Forum, 2014
Eileen Bernal, MD

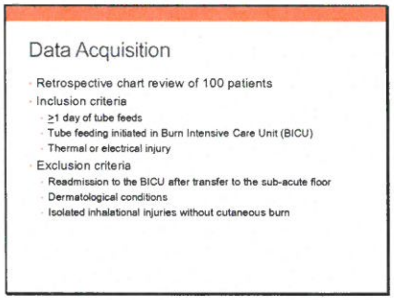
Slide 2



Nutrition in Burn Patients

- Higher nutritional needs
- Underfeeding is common
- Initiated during or immediately after resuscitation
- Enteral, parenteral, or both
- Only 70-80% of nutritional recommendations are met

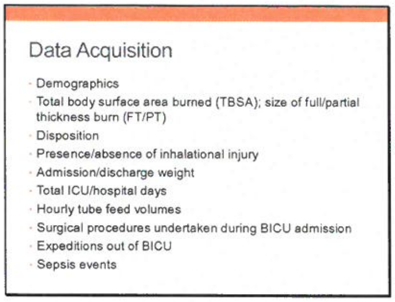
Slide 3



Data Acquisition

- Retrospective chart review of 100 patients
- Inclusion criteria
  - ≥1 day of tube feeds
  - Tube feeding initiated in Burn Intensive Care Unit (BICU)
  - Thermal or electrical injury
- Exclusion criteria
  - Readmission to the BICU after transfer to the sub-acute floor
  - Dermatological conditions
  - Isolated inhalational injuries without cutaneous burn

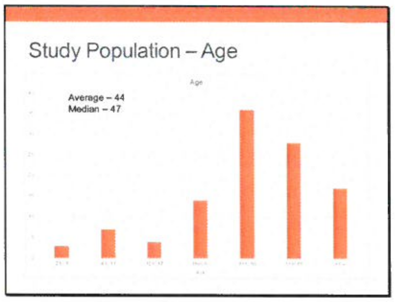
Slide 4



Data Acquisition

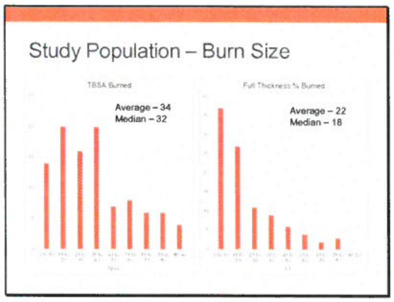
- Demographics
- Total body surface area burned (TBSA); size of full/partial thickness burn (FT/PT)
- Disposition
- Presence/absence of inhalational injury
- Admission/discharge weight
- Total ICU/hospital days
- Hourly tube feed volumes
- Surgical procedures undertaken during BICU admission
- Expeditions out of BICU
- Sepsis events

Slide 5



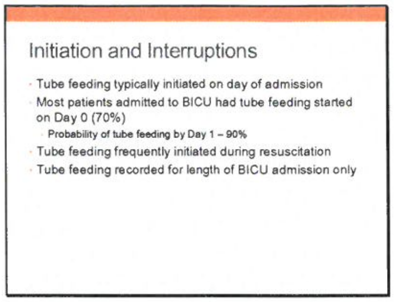
Study Population – Age

Slide 6



Study Population – Burn Size

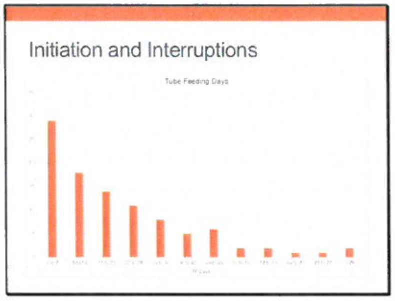
Slide 7



Initiation and Interruptions

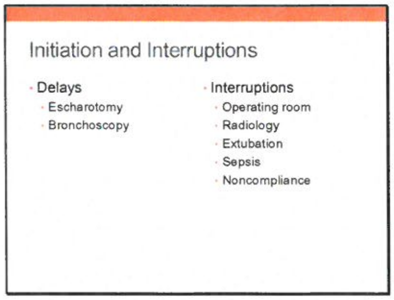
- Tube feeding typically initiated on day of admission
- Most patients admitted to BICU had tube feeding started on Day 0 (70%)
  - Probability of tube feeding by Day 1 – 90%
- Tube feeding frequently initiated during resuscitation
- Tube feeding recorded for length of BICU admission only

Slide 8



Initiation and Interruptions

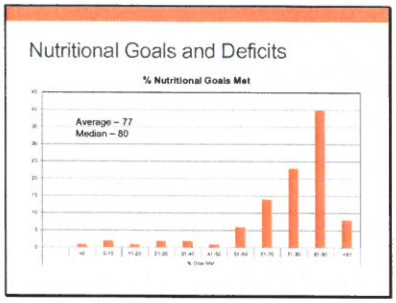
Slide 9



Initiation and Interruptions

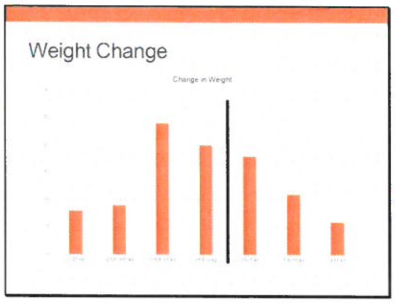
- Delays
  - Escharotomy
  - Bronchoscopy
- Interruptions
  - Operating room
  - Radiology
  - Extubation
  - Sepsis
  - Noncompliance

Slide 10



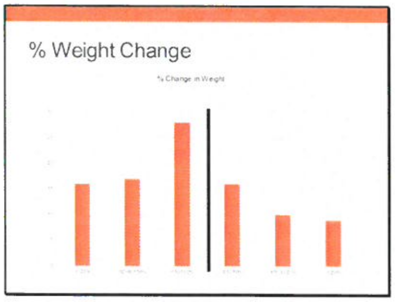
Nutritional Goals and Deficits

Slide 11



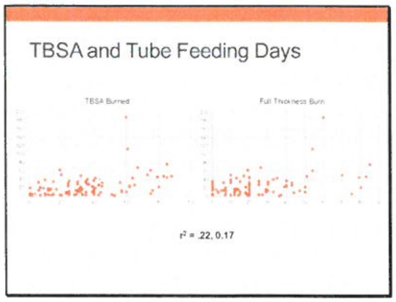
Weight Change

Slide 12



% Weight Change

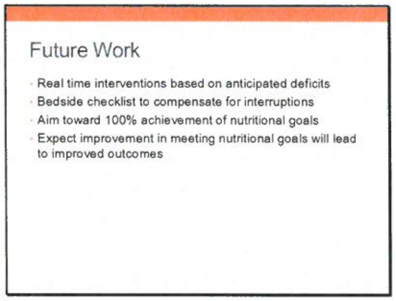
Slide 13



TBSA and Tube Feeding Days

r^2 = .22, 0.17

Slide 14



Future Work

- Real time interventions based on anticipated deficits
- Bedside checklist to compensate for interruptions
- Aim toward 100% achievement of nutritional goals
- Expect improvement in meeting nutritional goals will lead to improved outcomes

Abstract

Objective: In an effort to attenuate the hypermetabolic response that results from a severe burn injury, aggressive and early enteral nutrition is prescribed. Despite the best intent to treat, a trend of weight loss in adult patients has been observed, thus, a review of the medical record was undertaken.

Methods: Analyses were performed on 45 surviving burned patients, who were at least 18 years of age, and admitted to a burn center from 2009-2014. Nutritional intake and weights were analyzed for the first 30 days after admission. Change in weight over time was analyzed using a mixed linear model. Caloric deficit over time was analyzed using a generalized additive mixed model.

Results: Patients were an average of 44 years of age, 83 kg, and predominantly males with large burns. There was an average loss of weight by 14% within the first 30 days of hospitalization. When calories received were compared to calories recommended based on REE x 1.2, REE x 1.4, Curreri formula, and Galveston Adolescent formula a mean deficit of 1200, 1700, 2500, and 3000 calories were delivered per day, respectively.

Conclusion: Our results show that even with the best intent to treat, a substantial weight loss is occurring in acute burn patients within the first 30 days of admission. Additionally, the amount of calories delivered was found to be less than what is suggested. Improved vigilance of monitoring calories delivered may help decrease possible weight loss.

Key Words: burn; nutrition; calories; weight loss; hypermetabolic.

INTRODUCTION

Burn injuries result in the highest metabolic rate of any critical injury.[1] The metabolic response that follows a severe burn injury is identified as a hypermetabolic state. Such a state is characterized by a hyperdynamic cardiovascular response, increased energy expenditure, accelerated glycogen and protein breakdown, lipolysis, loss of lean body mass and body weight, delayed wound healing, and immune depression.[2,3] A net loss of protein post-burn results in muscle wasting and a decrease in lean body mass.[4,5] A significant decrease in body mass and lean body mass may result in consequences detrimental to the patient.[6]

One method to attenuate the hypermetabolic response is aggressive and early enteral feeding.[7,8] Several formulas have been created to address the postburn nutritional needs. Still, no one formula is perfect and some overestimate the number of calories needed by about 35-45%.[9,10] It has been found that through measuring REE via indirect calorimetry using bedside carts, a more accurate and individualized representation of the actual caloric requirements can be determined.[11,12] Still this method is not perfect.[12] It has been reported that feeding patients 1.2 times the measured REE leads to a 10% loss of lean body mass, but feeding patients 1.4 times the REE leads to an increase in fat deposition, but no increase in lean body mass.[11-13] Overfeeding has a myriad of detrimental effects, including, elevated respiratory quotients, increased fat synthesis, increased elimination of carbon dioxide, fat deposition in the liver, and hyperglycemia.[14-16] It can be concluded that determining a patient's accurate caloric requirement is necessary for positive clinical outcomes.[17]

A trend of weight loss has been observed in adult patients at the Blocker Burn Unit of the University of Texas Medical Branch in Galveston, Texas (UTMB), despite the best intent to treat. We hypothesize that this weight loss currently observed is secondary to delivery of insufficient calories relative to recommendations from nutritional formulas and calculations. Thus, a thorough examination of the medical record process has been undertaken.

METHODS

Subjects

Analyses were done on 45 burned patients, who were at least 18 years of age. The patients were admitted to UTMB from May 2009 to May 2014 for treatment. This research project was performed under a UTMB, Institutional Review Board, approved protocol.

Clinical Care

All subjects were admitted to the burn unit and treated in a similar manner by a team of three burn surgeons. Standard treatment included early excision of third degree burn wounds, and continuous enteral feeding. Early excision involves patients undergoing total burn wound excision and grafting within 48 hours of admission for any third degree burns. Patients returned to the operating room as donor sites healed and allowed for reharvesting of the unburned skin (usually 7 to 10 days). Additional surgical procedures for excision and grafting were undertaken until all wounds were covered and healed.

Each subject received continuous enteral nutrition delivered via nasoduodenal tube using Dobhoff tube starting shortly after admission using Vivonex TEN (Sandoz Nutrition Corporation, Minneapolis, MN). The composition of Vivonex is 82% carbohydrate, 15% protein, 3% fat. Daily caloric requirements were calculated using the Galveston Adolescent formula 1500 kcal/m^2 total body surface area + 1500 kcal/m^2 body surface area burned,[9] and orders were written to deliver calories at rates related to meet these requirements. Enteral feedings were continued until the patient could consume adequate calories from hospital trays necessary as calculated from the formula above. Patients were allowed to convert from tube-feeding to oral nutrition as tolerated.

Patients were on bedrest for 4 days after grafting and excision, and ambulated daily thereafter until the next excision and grafting procedure (7 to 14 days). Most patients underwent indirect calorimetry to determine resting energy expenditure (REE) within the first week of admission.

Study Design

To be included in this study, patients must have received at least one week of enteral tube feeding, no total parental nutrition, and had no major amputations during their acute hospitalization. Nutritional intake and weights were analyzed for the first 30 days after admission. The dry weight was documented as the lowest weight between admission and seven days after the first surgery. Weights were taken while the patient was nude. Patient weights and demographic information were collected from the electronic medical record.

The volume of tube-feeding delivered per hour was determined for each patient by reviewing the documentation in the electronic medical record. The concentration of tube-feeding was matched to the order that was written for the corresponding time. The volume delivered per day was calculated by summing those delivered between 7:00 AM and 6:59 AM the next day. The daily sums were determined this way as it was when the nurses, who recorded the volume of tube-feeding delivered, change shifts.

The daily volume of tube-feeding was multiplied by the concentration that was delivered throughout most of the 24 hour period. Vivonex TEN delivers one calorie per one milliliter, thus the resultant number (volume in ml x concentration) is equivalent to the number of calories delivered in one day. The number of calories delivered via tube-feeding from admission until day 30 was calculated for each patient each day. As the patient's wounds were healing, less tube-feeding was delivered in order to encourage eating a regular diet. At this point, only days when the patient received ≥ 90% of their calories via tube-feeding were included.

For the study, estimated calories recommended per day were calculated using the Curreri formula, the Galveston Adolescent formula, REE x 1.2, and REE x 1.4 (Table 1).[9,18-20] Each recommendation was compared to calories delivered.

Indirect Calorimetry

Indirect calorimetry was performed at a resting state in a standardized environmental setting of 30°C, the normal temperature of our patient rooms in the bun unit. REE was measured with a Sensor-Medics 2900 metabolic cart (Sensor-Medics, Yorba Linda, CA). Inspired and expired gases were collected and the composition was analyzed at sixty-second intervals. Carbon dioxide production, volume of and oxygen consumption values were reviewed and accepted when they were at a steady state for at least five minutes. From these measurements, the average REE was then calculated.

Data Analysis

Patient demographics were summarized as means with standard deviations for continuous variables, or as counts with corresponding percentages for categorical variables. Patient weight over time was modeled by a mixed linear model, adjusting for the covariates dry weight, TBSA, age, gender, and presence of inhalation injury, while blocking on subject to account for repeated measures. Percentage of dry weight and calories delivered over time were each modeled similarly.

Differences between calories delivered by tube-feeding and the recommendations by each formula were separately modeled as a function of days post-admission by a generalized additive mixed model, blocking on subject, and accounting for the non-linear relation between calorie difference and day. [21] The same differences were also modeled simultaneously as a function of days post-admission and feeding formula with an interaction between days and formula, blocking on subject. Statistical analyses were performed using R statistical software (R Core Team, 2013, version 3.0.1).[22] A 95% level of confidence was assumed.

RESULTS

Patients Studied

Table 2 summarized patient demographics. This study included 45 patients who were about 44 years of age and predominantly male. They had an average TBSA burned of 41% with 22% 3rd degree burned. The patients had an average length of stay of 37 days and stayed approximately one day per percent burn (Table 2).

Effects on Weight

Mean weights declined by approximately 11 kg, as summarized in Figure 1. The model shows that each kilogram increase in dry weight was associated with a mean retention of 0.9 kilogram ($p < 0.0001$). Each additional day was associated with a 0.4 kilogram decrease in weight ($p < 0.0001$).

During the initial 30 days following admission, mean weights declined by approximately 14%, as summarized in Figure 2. The model shows that each kilogram increase in dry weight was associated with a mean retention of 1.6 percent higher weight ($p < 0.0001$). Each additional day was associated with a 0.5 percent decrease in weight ($p < 0.0001$).

Calories Delivered

Calories delivered over time are summarized in Figure 3. There was a significant relation with dry weight ($p = 0.045$), total body surface area burned ($p = 0.013$), age ($p = 0.027$), and presence of inhalation injury ($p = 0.0015$) to calories delivered. Each 1 kg increase in dry weight was associated with 15 additional calories delivered. Each 1% increase in TBSA was associated with 16 additional calories delivered. Each 1 year increase in age was associated with 17 additional calories delivered. The presence of an inhalation injury was associated with 611 additional calories delivered.

Differences between actual calories delivered and the recommendations by REE x 1.2, REE x 1.4, the Curreri formula, and the Galveston formula are summarized in Figure 4 as functions of days post-admission. The mean deficit per patient was 1200, 1700, 2500, and 3000 calories per day, respectively. The caloric deficits were greatest in the first few days following admission.

DISCUSSION

There are a variety of formulas that have been created to maintain body weight in patients after a severe burn.[23] This array of formulas implies that no one formula is particularly better than another when it comes to feeding burned patients. Although, there is not a set amount of calories that should be delivered to burned patients, there is one goal which should be met: catabolism should be decreased, such that the patient does not lose weight.[17]

It has been shown that with aggressive and early enteral feeding catabolism is attenuated.[7,8] In order to estimate the amount of calories recommended to adults with massive burns, one can use the Curreri formula, which is stratified based on age.[18] At our institution, we use the Galveston Adolescent formula,[9] which recommends more calories than the Curreri formula,[18] and is more user-friendly. Additionally, REE can be used in combination with the Galveston formula in order to find a balance between the formula estimation and the calculated estimation. At our institution, calories are ordered at 1.2 to 1.4 x REE. Recommendations in the literature vary from 0.8 to 2.0 x REE.[11-13,24]

It should be noted that formulas are estimations of caloric needs, which can be affected by a variety of clinical events. Overall, this rate of tube-feeding is well accepted, but at times patients are unable to tolerate it leading to the delivery of fewer calories. In this study, patients with massive burns lost approximately 14% of their dry weight within 30 days of admission. This correlates with a deficit of approximately 1200-2500 calories delivered per day. It was found that with each 1 kg increase in dry weight only 15 additional calories were delivered, when according to the Curreri formula 25 kilocalories should have been delivered for every kilogram increase. Similarly, with each 1% increase in TBSA burned only 16 additional calories were delivered, when 40 kilocalories per percent should have been delivered according to Curreri.[18]

The current illustration of the inadequacy of caloric delivery seems remarkable. The insufficiencies may be explained by, the practice of stopping tube feeding for surgery, wound care, research studies, clinical testing, and other interruptions. This practice may explain the deficit of calories delivered, and may be inevitable. Although, when tube-feeding is turned off, the amount of calories missed during that time should be made up throughout the rest of the day.

In order to address this issue, adjustments to current formulas, practices, or tabulations, may be needed to account for times without tube-feeding. Education and vigilance are important in order to assure nutrition orders are followed and that each patient receives the nutrition and calories they require. In burn units, food has often been called medicine to a burn patient, such that, it is necessary and serves a purpose for their recovery. For example, it attenuates the hypermetabolic state, improves wound healing, decreases catabolism, and increases the chance of survival.[7,8,25,26] Since nutrition plays such a substantial role to burn patients, it is imperative that adequate formulas be utilized and daily monitoring of total intake, not just rate delivered hourly, be performed.[17]

ACKKNOWLEDGMENTS

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REFERENCES

1. Yarborough M, Herndon D, Curreri P. Nutritional management of the severely injured patient. *Contemporary Surgery.* 1978;13:15-20.
2. Lee JO, Herndon DN. Modulation of the post-burn hypermetabolic state. *Nestle Nutrition workshop series. Clinical & performance programme.* 2003;8:39-49; discussion 49-56.
3. Herndon D. Mediators of metabolism. *The Journal of trauma.* 1981;21(701-705).
4. Jeschke MG, Chinkes DL, Finnerty CC, et al. Pathophysiologic response to severe burn injury. *Annals of surgery.* Sep 2008;248(3):387-401.
5. Hart DW, Wolf SE, Mlcak R, et al. Persistence of muscle catabolism after severe burn. *Surgery.* Aug 2000;128(2):312-319.
6. Chang DW, DeSanti L, Demling RH. Anticatabolic and anabolic strategies in critical illness: a review of current treatment modalities. *Shock.* Sep 1998;10(3):155-160.
7. Dominioni L, Trocki O, Fang CH, et al. Enteral feeding in burn hypermetabolism: nutritional and metabolic effects of different levels of calorie and protein intake. *JPEN. Journal of parenteral and enteral nutrition.* May-Jun 1985;9(3):269-279.
8. Mochizuki H, Trocki O, Dominioni L, Brackett KA, Joffe SN, Alexander JW. Mechanism of prevention of postburn hypermetabolism and catabolism by early enteral feeding. *Annals of surgery.* Sep 1984;200(3):297-310.
9. Hildreth MA, Herndon DN, Desai MH, Duke MA. Caloric needs of adolescent patients with burns. *The Journal of burn care & rehabilitation.* Nov-Dec 1989;10(6):523-526.
10. Hildreth MA, Herndon DN, Parks DH, Desai MH, Rutan T. Evaluation of a caloric requirement formula in burned children treated with early excision. *The Journal of trauma.* Feb 1987;27(2):188-189.
11. Goran MI, Peters EJ, Herndon DN, Wolfe RR. Total energy expenditure in burned children using the doubly labeled water technique. *The American journal of physiology.* Oct 1990;259(4 Pt 1):E576-585.
12. Gore DC, Rutan RL, Hildreth M, Desai MH, Herndon DN. Comparison of resting energy expenditures and caloric intake in children with severe burns. *The Journal of burn care & rehabilitation.* Sep-Oct 1990;11(5):400-404.
13. Hart DW, Wolf SE, Herndon DN, et al. Energy expenditure and caloric balance after burn: increased feeding leads to fat rather than lean mass accretion. *Annals of surgery.* Jan 2002;235(1):152-161.
14. Askanazi J, Rosenbaum SH, Hyman AI, Silverberg PA, Milic-Emili J, Kinney JM. Respiratory changes induced by the large glucose loads of total parenteral nutrition. *JAMA : the journal of the American Medical Association.* Apr 11 1980;243(14):1444-1447.
15. Klein CJ, Stanek GS, Wiles CE, 3rd. Overfeeding macronutrients to critically ill adults: metabolic complications. *Journal of the American Dietetic Association.* Jul 1998;98(7):795-806.
16. Saffle JR, Graves C, Cochran A. Nutritional support of the burned patient. In: Herndon D, ed. *Total Burn Care.* London: Saunders Elsevier; 2012.
17. Newsome TW, Mason AD, Jr., Pruitt BA, Jr. Weight loss following thermal injury. *Annals of surgery.* Aug 1973;178(2):215-217.
18. Curreri PW, Richmond D, Marvin J, Baxter CR. Dietary requirements of patients with major burns. *Journal of the American Dietetic Association.* Oct 1974;65(4):415-417.
19. Saffle JR, Medina E, Raymond J, Westenskow D, Kravitz M, Warden GD. Use of indirect calorimetry in the nutritional management of burned patients. *The Journal of trauma.* Jan 1985;25(1):32-39.
20. Turner WW, Jr., Ireton CS, Hunt JL, Baxter CR. Predicting energy expenditures in burned patients. *The Journal of trauma.* Jan 1985;25(1):11-16.
21. Wood S. *Generalized additive models: an introduction with R.*: CRC Press; 2006.
22. *R: a language and environment for statistical computing.* [computer program]. Version 3.0.1. Vienna, Austria: R Foundation for Statistical Computing; 2013.
23. Lee JO, Benjamin D, Herndon DN. Nutrition support strategies for severely burned patients. *Nutrition in clinical practice : official publication of the American Society for Parenteral and Enteral Nutrition.* Jun 2005;20(3):325-330.
24. Williams FN, Herndon DN, Jeschke MG. The hypermetabolic response to burn injury and interventions to modify this response. *Clinics in plastic surgery.* Oct 2009;36(4):583-596.
25. Hart DW, Wolf SE, Chinkes DL, et al. Effects of early excision and aggressive enteral feeding on hypermetabolism, catabolism, and sepsis after severe burn. *The Journal of trauma.* Apr 2003;54(4):755-761; discussion 761-754.

26. Mosier MJ, Pham TN, Klein MB, et al. Early enteral nutrition in burns: compliance with guidelines and associated outcomes in a multicenter study. *Journal of burn care & research : official publication of the American Burn Association.* Jan-Feb 2011;32(1):104-109.

Table 1. Formulas and calculations used to estimate calories required to maintain body weight in a burned patient.

Table 2. Demographics of patients included in this study.

Figure 1. Adjusted mean weight over time. Shaded regions indicate 95% confidence intervals.

Figure 2. Adjusted mean percentage of dry weight over time. Shaded regions indicate 95% confidence intervals.

Figure 3. Adjusted mean tube-fed calories given over time. Shaded regions indicate 95% confidence intervals.

Figure 4. Differences between calories delivered by tube feeding and calories recommended per formula. The shaded regions span the standard error. REE = resting energy expenditure.

Table 1. Formulas and calculations used to estimate calories required to maintain body weight in a burned patient.

	Age Range (years)	Formula / Calculation
Galveston	12 - 16	1500 kcal / m^2 TBSA + 1500 kcal / m^2 TBSA burned
Curreri	16 - 59	25 kcal / kg of weight + 40 kcal / (% TBSA)
Curreri	≥ 60	20 kcal / kg of weight + 65 kcal / (% TBSA)
REE	Any	Typically 1.2 - 1.6 x REE

TBSA = total body surface area

REE = resting energy expenditure

Table 2. Demographics of patients included in this study.

Variable	Value
n	45
Age, years	44 ± 16
Gender, males (%)	35 (78%)
LOS, days	37 ± 25
TBSA burn, %	41 ± 17
3^{rd} burn, %	22 ± 21
Day / % burn, day	1.0 ± 0.4

LOS = length of stay
TBSA = total body surface area
Data presented as means ± SD, or counts (%).

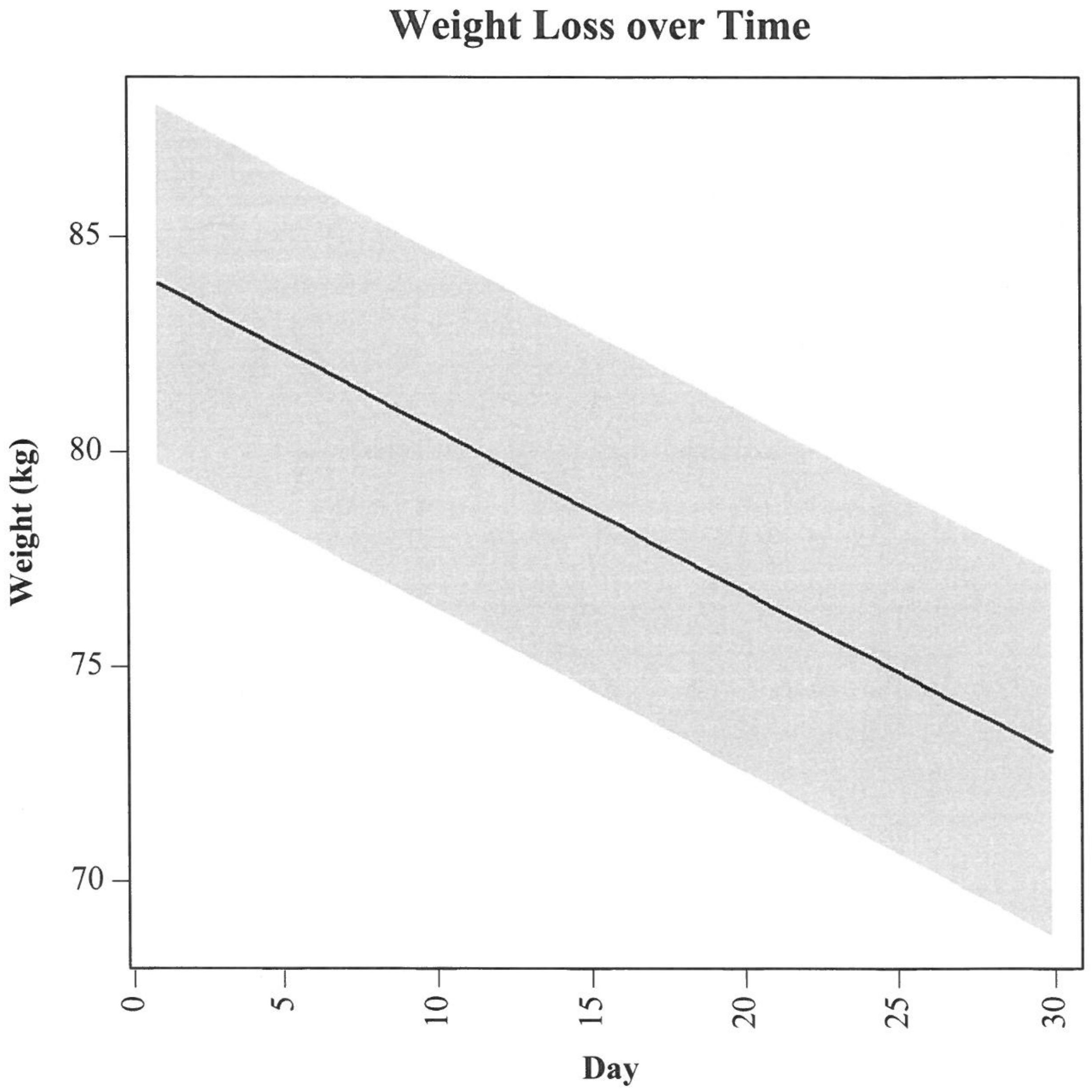

Figure 1. Adjusted mean weight over time. Shaded regions indicate 95% confidence intervals.

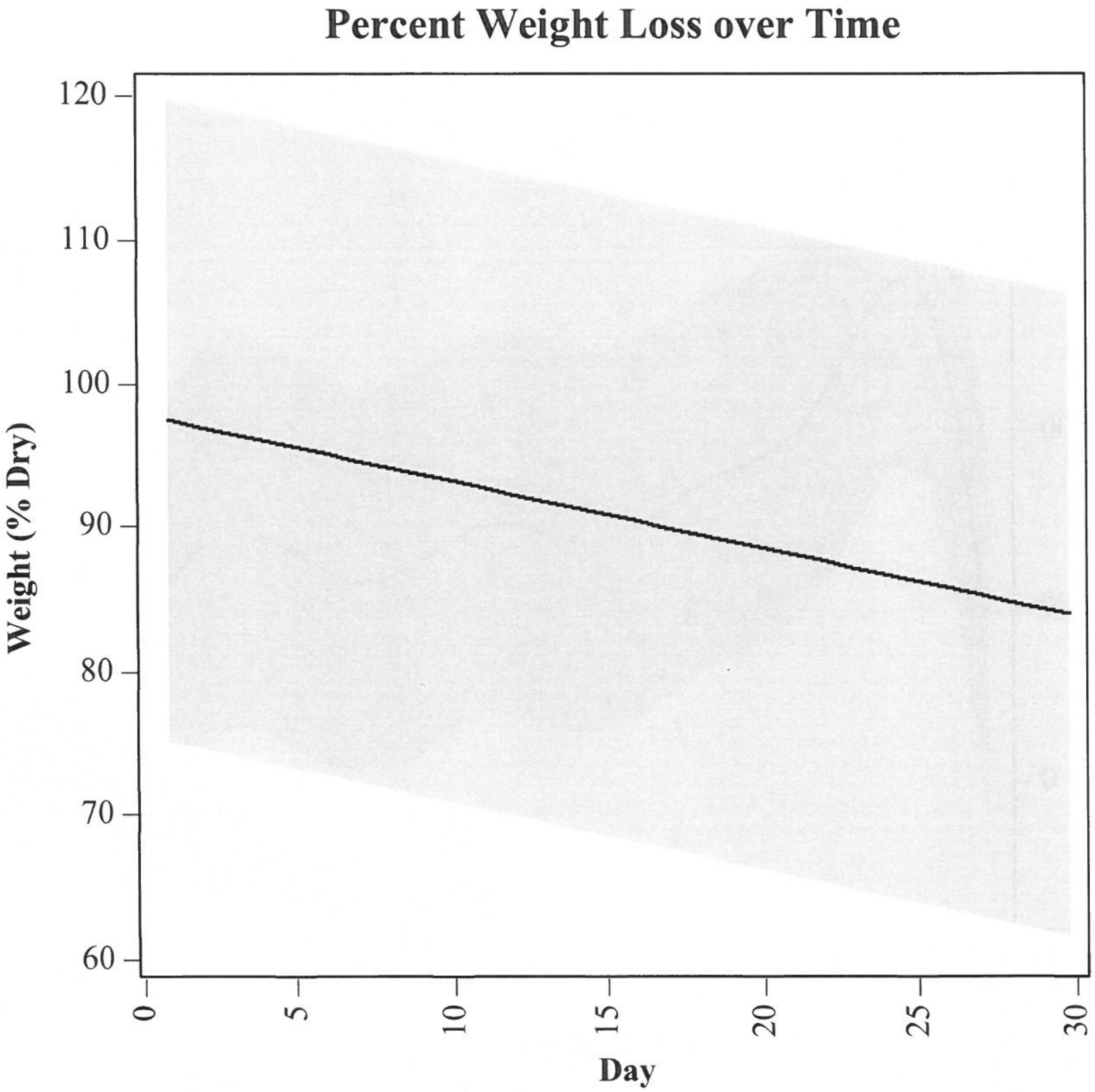

Figure 2. Adjusted mean percentage of dry weight over time. Shaded regions indicate 95% confidence intervals.

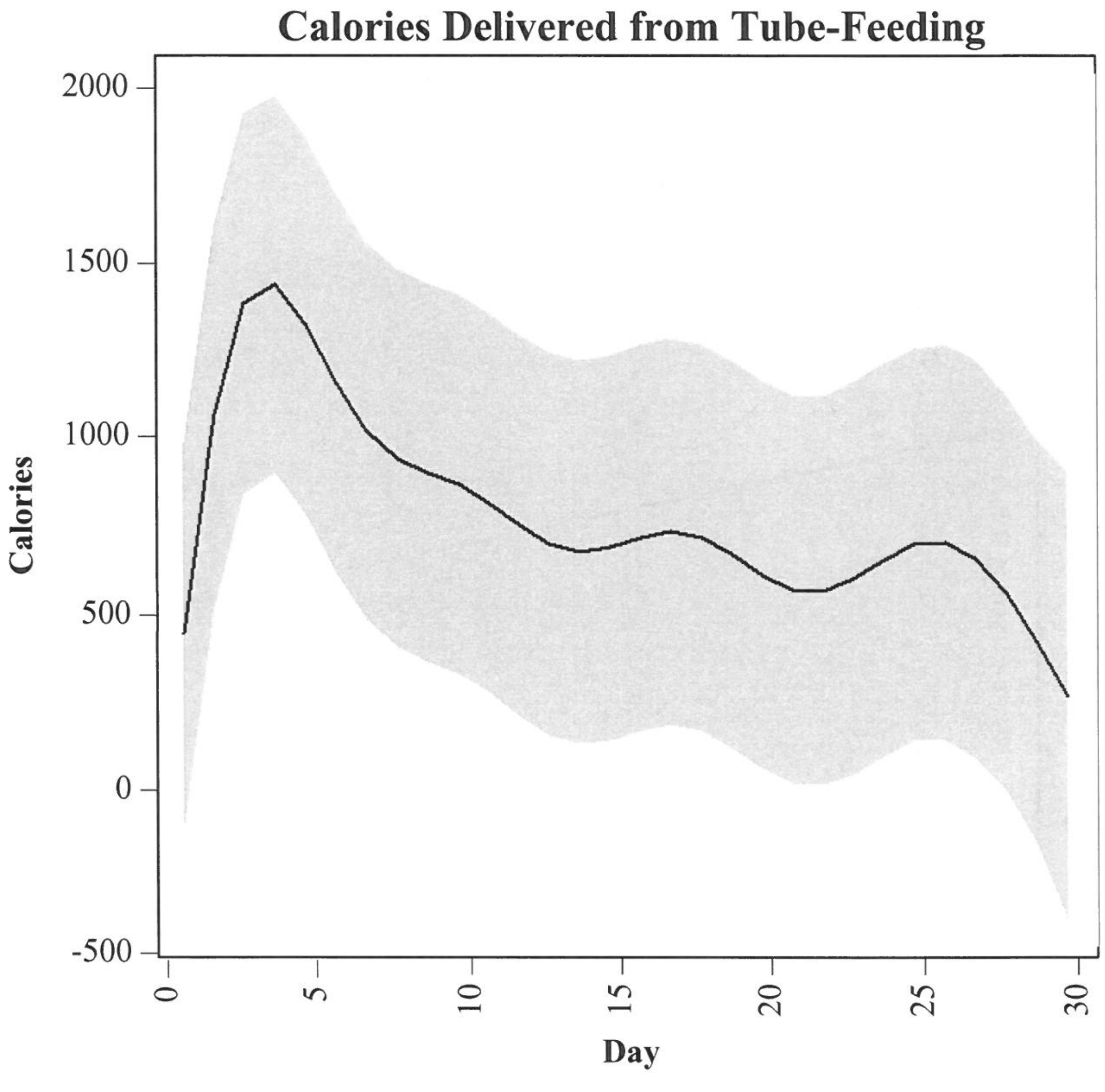

Figure 3. Adjusted mean tube-fed calories given over time. Shaded regions indicate 95% confidence intervals.

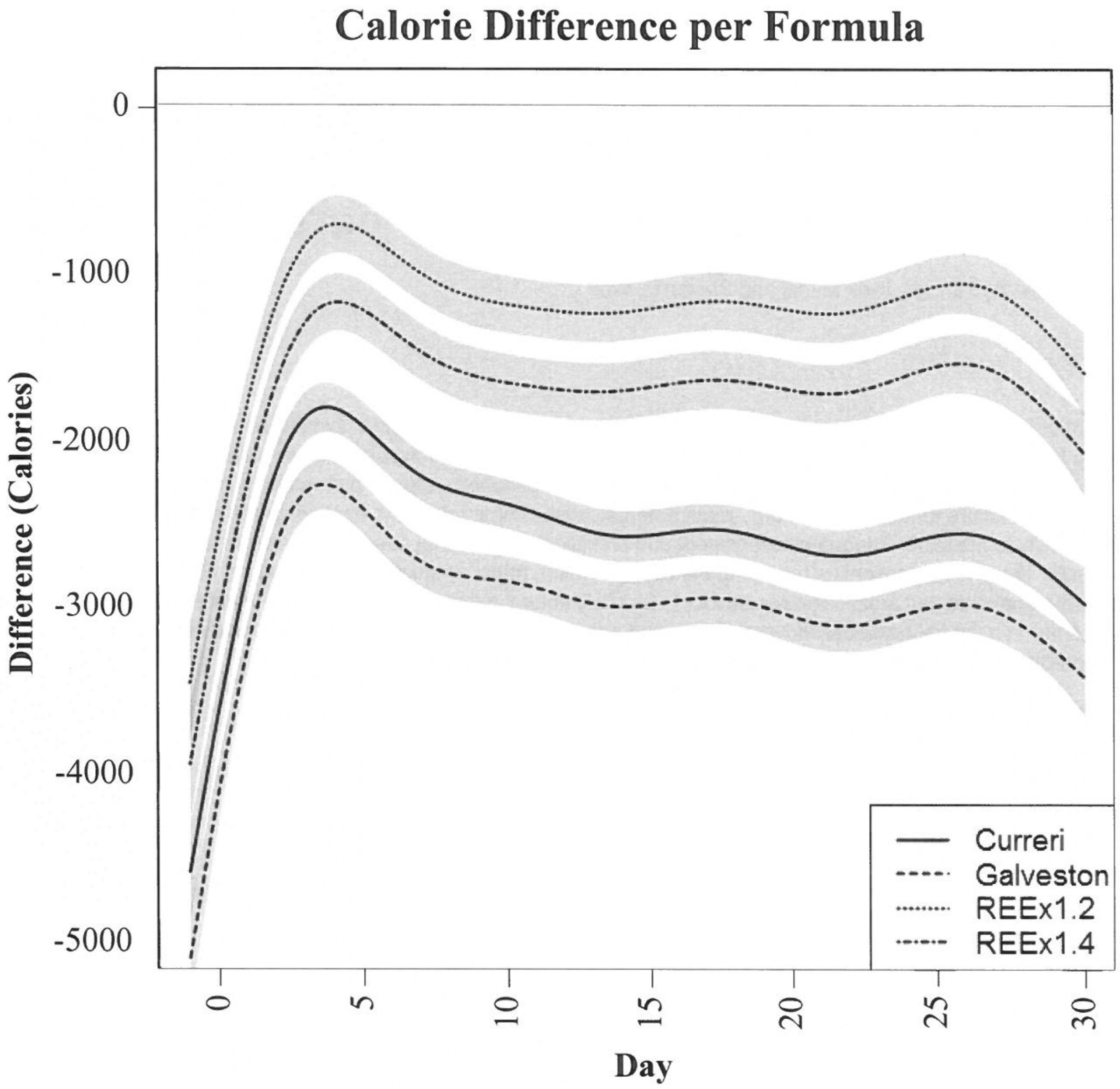

Figure 4. Differences between calories delivered by tube feeding and calories recommended per formula. The shaded regions span the standard error. REE = resting energy expenditure.

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Burns & Trauma

REVIEW Open Access

Nutrition and metabolism in burn patients

Audra Clark*, Jonathan Imran, Tarik Madni and Steven E. Wolf

Abstract

Severe burn causes significant metabolic derangements that make nutritional support uniquely important and challenging for burned patients. Burn injury causes a persistent and prolonged hypermetabolic state and increased catabolism that results in increased muscle wasting and cachexia. Metabolic rates of burn patients can surpass twice normal, and failure to fulfill these energy requirements causes impaired wound healing, organ dysfunction, and susceptibility to infection. Adequate assessment and provision of nutritional needs is imperative to care for these patients. There is no consensus regarding the optimal timing, route, amount, and composition of nutritional support for burn patients, but most clinicians advocate for early enteral nutrition with high-carbohydrate formulas. Nutritional support must be individualized, monitored, and adjusted throughout recovery. Further investigation is needed regarding optimal nutritional support and accurate nutritional endpoints and goals.

Keywords: Burn, Nutrition, Metabolism, Critical care

Background

Nutritional support is a critical aspect of the treatment of burn patients. The metabolic rate of these patients can be greater than twice the normal rate, and this response can last for more than a year after the injury [1, 2]. Severe catabolism accompanies the hypermetabolic state and leads to a tremendous loss of lean body mass as well as a decline of host immune function [3]. Significant nu- tritional support to meet increased energy expenditure is vital for burn patients' survival. Unfortunately, our know- ledge regarding the complicated physiology of nutrition is incomplete and nutritional regimens vary widely between individual centers. Many questions still exist concerning the optimal route, volume, and composition of diet in the burn population. This article will review the current state of nutrition after burn injury.

Review

The hypermetabolic state

Severe burns cause a profound pathophysiological stress response and a radically increased metabolic rate that can persist for years after injury. Trauma and sepsis also result in hypermetabolism, although to a much lesser degree and for a significantly shorter duration (Fig. 1). Immediately after severe injury, patients have a period of decreased metabolism and reduced tissue perfusion known as the "ebb" phase. Soon after, they enter the phase of hypermetabolic rates and hyperdynamic circu- lation, referred to as the "flow" state [4]. This hypermet- abolic state reflects an increase in whole-body oxygen consumption, and a patient is usually considered hypermetabolic when resting energy expenditure (REE) is more than 10% above normal [5]. In the acute postburn injury phase, patients with a burn that covers greater than 40% of total body surface area (TBSA) have a REE between 40 and 100% above normal [6, 7]. It is import- ant to mitigate this stress response and support the sig- nificantly increased metabolic needs of the patient as unchecked hypermetabolism results in an enormous loss of lean muscle mass, immune compromise, and delayed wound healing.

Hypermetabolism after burn is very complicated and not yet fully understood. The underlying mechanisms of this vast metabolic, hormonal, and inflammatory dysregulation are still being actively investigated. At a cellular level, increased whole-body oxygen consumption supports greater adenosine triphosphate (ATP) turnover and thermogenesis. ATP-consuming reactions represent an estimated 57% of the hypermetabolic response to burns, including ATP turnover for protein synthesis, ATP production for hepatic gluconeogenesis, and the cycling of glucose and fatty acids [8]. Because ATP turn- over does not completely account for burn-induced

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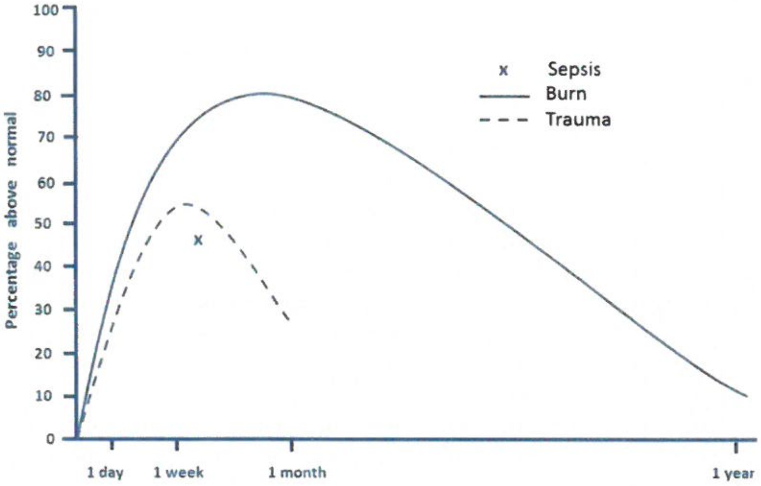

Fig. 1 Hypermetabolic response after severe burn, trauma, and sepsis. Adapted from references [5, 6, 123, 124]

hypermetabolism, it implies that mitochondrial oxygen consumption exceeds ATP production after severe burn. This likely occurs via the uncoupling of mitochondrial respiration from ADP phosphorylation resulting in heat production [5]. This theory is supported by the recent finding that uncoupling protein 1 (UCP1), a mitochon- drial transmembrane protein and a principal mediator of thermogenesis, is much more abundant in the adipose tissue of burn patients compared to healthy individuals [9, 10].

Several studies implicate catecholamines as a primary mediator of hypermetabolism [11, 12]. The elevation of catabolic hormones epinephrine, cortisol, and glucagon lead to the inhibition of protein synthesis and lipogen- esis [13]. Protein breakdown becomes a necessary and large source of energy, and skeletal muscle cachexia re- sults from a long-lasting imbalance between protein syn- thesis and breakdown. The dysregulation of skeletal muscle kinetics lasts a year or more after severe burn, and reduced lean body mass is reported in patients up to 3 years after injury [14–16].

Adequate and prompt nutrition is extremely important for preventing numerous complications, although nutri- tion has a complex relationship with the hypermetabolic state. In animal models, early nutrition, usually defined as within 24 h of injury, has been shown to actually miti- gate burn-induced hypercatabolism and hypermetabo- lism, although data in humans have not borne this out [17, 18]. A study by Hart et al. compared burned chil- dren who had early aggressive feeding and wound exci- sion to burned children who had delay to this treatment, with the authors expecting to find that early surgical treatment and aggressive enteral nutritional support would limit the hypermetabolic response to burn. Sur- prisingly, they found that the late treatment cohort had significantly lower energy expenditure than the early treatment group. Furthermore, the children with delayed nutrition and surgical excision had a significant increase in their energy expenditure after the initiation of ther- apy. The authors concluded that excision and aggressive feeding are requisite for the full expression of burn- induced hypermetabolism. Muscle protein catabolism, on the other hand, was significantly decreased in the pa- tients who received early treatment [19]. Burn patients are in a catabolic state that can lead to significant weight loss and associated complications. A 10% loss of total body mass leads to immune dysfunction, 20% to im- paired wound healing, 30% to severe infections, and 40% to mortality [20]. Early enteral feeding does result in im- proved muscle mass maintenance, the modulation of stress hormone levels, improved gut mucosal integrity, improved wound healing, decreased risk of Curling ulcer formation, and shorter intensive care unit stay and is therefore universally recommended despite its link to the hypermetabolic state [21, 22].

Many other therapies to ameliorate burn-induced hypermetabolism have been investigated. Environmental management with the warming of patients' rooms and occlusive wound dressings attenuate the hypermetabolic response because burn patients have lost their skin barrier and therefore need to produce more heat to maintain thermal neutrality. Early wound excision and grafting have led to improvements in mortality, decreased exudative protein loss, lower risk of burn wound infection, and decreased muscle catabolism [19, 23]. This may be due to a decrease in the levels of circulating inflammatory cytokines such as interleukin (IL)-6, IL-8, C3 complement, and tumor necrosis factor (TNF)-α [24].

Several proven pharmacologic methods can be used to decrease the hypermetabolic response to burn. Beta-adrenergic receptor blockade, usually with propranolol, lowers the heart rate and metabolic rate in patients with severe burns [25–27]. Recently, propranolol treatment for 1-year postburn was shown to improve peripheral lean body mass accumulation [28]. Oxandrolone, a syn- thetic androgen, has been shown to blunt hypermetabo- lism, improve bone mineral content and density, and increase the accretion of lean body mass in children with severe burn [29–32]. Recombinant human growth hormone (rHGH) has been found to reduce hyperme- tabolism and improve lean body mass accretion after burn, but its use has been limited because of two multi- center trials showing that growth hormone therapy in- creased mortality in critically ill adults [33–35]. More research is needed regarding the efficacy and safety of rHGH use in burn patients.

Timing of nutritional support

Time to treatment, including time to nutrition, is an important factor for patient outcome after severe burn. Substantial intestinal mucosal damage and increased bacterial translocation occur after burn and result in decreased absorption of nutrients [36]. Because of this, nutritional support should ideally be initiated within 24 h of injury via an enteral route [2, 19]. In animal models, early enteral feeding has been shown to significantly at- tenuate the hypermetabolic response after severe burn. Mochizuki et al. demonstrated that guinea pigs who were continuously fed enterally starting at 2 h after burn had a significant decrease in metabolic rate at 2 weeks after burn compared to animals whose nutrition was ini- tiated 3 days after burn [17]. This improvement of the hypermetabolic response has not borne out in human studies; however, early enteral nutrition (EN) has been shown to decrease circulating catecholamines, cortisol, and glucagon and preserve intestinal mucosal integrity, motility, and blood flow [18, 37–40]. Early enteral feed- ing in humans has also shown to result in improved muscle mass maintenance, improved wound healing, de- creased risk of Curling ulcer formation, and shorter in- tensive care unit stay [21, 22]. Nutrition, both parenteral and enteral, is almost always administered in a continu- ous fashion. For parenteral nutrition (PN), this is done for logistical reasons, but reasons for continuous feeding are less clear for EN. At the start, enteral feeding is initi- ated in a continuous and low volume manner with slow titration to the goal volume to insure that the patient can tolerate this regimen. A continuous schedule is usu- ally continued even when the patient is having no issues with tolerance. Continuous enteral feeding is likely a holdover from parenteral schedules and no data have shown the superiority of either schedule, but the data are limited [41]. Normal physiology functions with inter- mittent feeding usually during daytime hours, and fur- ther research is needed to determine if there might be a benefit to intermittent feeding after burn.

Caloric requirements

The primary goal of nutritional support in burn patients is to fulfill the increased caloric requirements caused by the hypermetabolic state while avoiding overfeeding. Numerous formulas to estimate the caloric needs of burn victims have been developed and used throughout the years [42]. One of the earliest examples is the Curreri formula [43]. It was proposed in 1972 and created by studying 9 patients and computing backwards to ap- proximate the calories that would have been needed to compensate for the patients' weight loss. The Curreri formula and many other older formulas overestimate current metabolic requirements, and more sophisti- cated formulas with different variables have been pro- posed (Table 1) [44]. One study of 46 different formulas for predicting caloric needs in burn patients found that none of them correlated well with the measured energy expenditure in 24 patients [1]. Energy expenditure does fluctuate after burn, and fixed formulas often lead to underfeeding during periods of highest energy utilization and to overfeeding late in the treatment course.

Indirect calorimetry (IC) is the current gold standard for the measurement of energy expenditure, but it is not practical to perform on a routine basis. IC ma- chines measure the volume of expired gas and the in- haled and exhaled concentrations of oxygen and carbon dioxide via tight-fitting face masks or ventilators, allow- ing for the calculation of oxygen consumption (VO_2) and carbon dioxide production (VCO_2), and therefore metabolic rate [45]. IC can also detect underfeeding or overfeeding by calculation of the respiratory quotient (RQ), which is the ratio of carbon dioxide produced to oxygen consumed (VCO_2/VO_2) [42]. This ratio is af- fected by the body's metabolism of specific substrates. In unstressed starvation, fat is utilized as a major en- ergy source which produces an RQ of <0.7. The normal metabolism of mixed substrates yields an RQ of around 0.75–0.90. Overfeeding is typified by the synthesis of fat from carbohydrate resulting in an RQ of >1.0. This ex- plains one feared complication of overfeeding: diffi- cultly weaning from ventilatory support [46]. Despite this concern, one study found that high-carbohydrate diets in a group of pediatric burn patients led to de- creased muscle wasting and did not result in RQs over 1.05 or any respiratory complications [47].

Substrates

The metabolic process involves the creation and degradation of many products necessary for biological processes. Metabolism of three macronutrients—carbohydrates, proteins, and lipids—provide energy via different pathways (Fig. 2).

Table 1 Common formulas used to calculate caloric needs of burn patients

Adult formulas	Kcal/day	Comments
Harris Benedict	Men: 66.5 + 13.8(weight in kg) + 5(height in cm) − 6.76(age in years) Women: 655 + 9.6(weight in kg) + 1.85(height in cm) − 4.68(age in years)	Estimates basal energy expenditure; can be adjusted by both activity and stress factor, multiply by 1.5 for common burn stress adjustment
Toronto Formula	−4343 + 10.5(TBSA) + 0.23(calorie intake in last 24 h) + 0.84(Harris Benedict estimation without adjustment) + 114(temperature) − 4.5(number of postburn days)	Useful in acute stage of burn care; must be adjusted with changes in monitoring parameters
Davies and Lilijedahl	20(weight in kg) + 70(TBSA)	Overestimates caloric needs for large injuries
Ireton-Jones	Ventilated patient: 1784 − 11 (age in years) + 5 (weight in kg) + (244 if male) + (239 if trauma) + (804 if burn) Non-ventilated patient: 629 − 11 (age in years) + 25 (weight in kg) − (609 if obese)	Complex formula which integrates variables for ventilation and injury status
Curreri	Age 16–59: 25(weight in kg) + 40(TBSA) Age >60: 20(weight in kg) + 65(TBSA)	Often overestimates caloric needs
Pediatric formulas		
Galveston	0–1 year: 2100(body surface area) + 1000(body surface area × TBSA) 1–11 year: 1800(body surface area) + 1300(body surface area × TBSA) 12–18 years: 1500(body surface area) + 1500(body surface area × TBSA)	Focuses on maintaining body weight
Curreri junior	<1 year: recommended dietary allowance + 15(TBSA) 1–3 years: recommended dietary allowance + 25(TBSA) 4–15 years: recommended dietary allowance + 40(TBSA)	Commonly overestimates caloric needs

TBSA total body surface area

Carbohydrates

Carbohydrates are the favored energy source for burn patients as high-carbohydrate diets promote wound healing and impart a protein-sparing effect. A randomized study of 14 severely burned children found that those receiving a high-carbohydrate diet (in comparison to a high-fat diet) had significantly less muscle protein degradation [48]. This makes carbohydrates an extremely important part of the burn patient's diet; however, there is a maximum rate at which glucose can be oxidized and used in severely burned patients (7 g/kg/day) [49, 50]. This rate can be less than the caloric amount needed to prevent lean body mass loss, meaning severely burned patients may have greater glucose needs than can be safely given. If glucose is given in excess of what can be utilized, it leads to hyperglycemia, the conversion of glucose to fat, glucosuria, dehydration, and respiratory problems [51].

The hormonal environment of stress and acute injury causes some level of insulin resistance, and many patients benefit from supplemental insulin to maintain satisfactory blood sugars. Insulin therapy also promotes muscle protein synthesis and wound healing [52]. Studies have found that severely burned patients who received insulin infusions, in conjunction with a high-carbohydrate, high-protein diet, have improved donor site healing, lean body mass, bone mineral density, and decreased length of stay [53, 54]. Hypoglycemia is a serious side effect of insulin therapy, and patients must be monitored closely to avoid this complication.

Fat

Fat is a required nutrient to prevent essential fatty acid deficiency, but it is recommended only in limited amounts [13]. After burn, lipolysis is suppressed and the utilization of lipids for energy is decreased. The increased beta-oxidation of fat provides fuel during the hypermetabolic state; however, only 30% of the free fatty acids are degraded and the rest go through reesterification and accumulate in the liver. Additionally, multiple studies suggest that increased fat intake adversely affects immune function [55, 56]. Because of these effects, many authorities recommend very low-fat diets (<15% of total calories) in burn patients where no more than 15% of total calories come from lipids. Multiple low-fat enteral formulas have been created for this purpose, and for

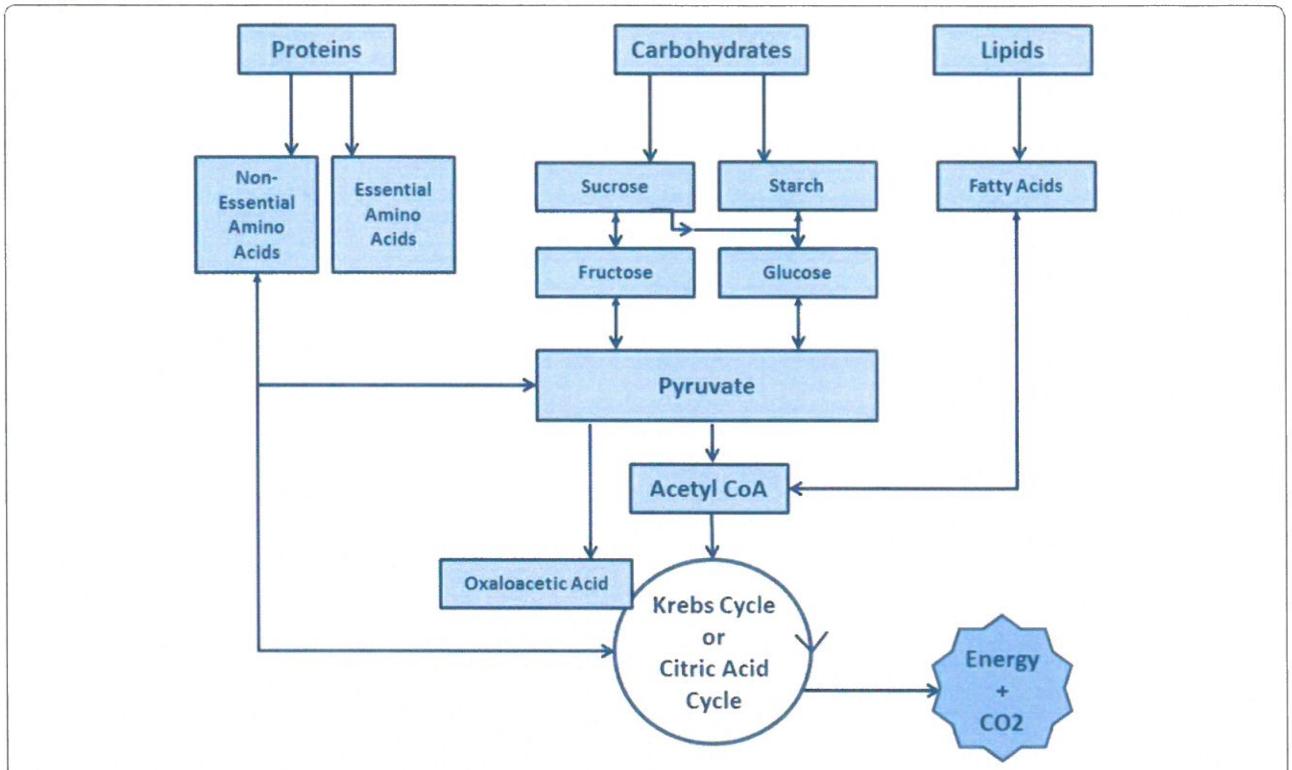

Fig. 2 Metabolism of protein, carbohydrates, and lipids

patients receiving short-term (<10 days) PN, many clinicians forego lipid emulsions.

In addition to the amount of fat, the composition of administered fat must be considered. The most commonly used formulas contain omega-6 fatty acids such as linoleic acid, which are processed via the synthesis of arachidonic acid, a precursor of proinflammatory cytokines (e.g., prostaglandin E_2). Lipids that contain a high percentage of omega-3 fatty acids are metabolized without promoting proinflammatory molecules and have been linked to enhanced immune response, reduced hyperglycemia, and improved outcomes [57, 58]. Because of this, omega-3 fatty acids are a major component of "immune-enhancing diets." Most enteral formulas have an omega 6:3 ratio between 2.5:1 and 6:1 while the immune-enhancing diets have an omega 6:3 ratio closer to 1:1. The ideal composition and amount of fat in nutritional support for burn patients remains a topic of controversy and warrants further investigation.

Protein

Proteolysis is greatly increased after severe burn and can exceed a half pound of skeletal muscle daily [59]. Protein supplementation is needed to meet ongoing demands and supply substrate for wound healing, immune function, and to minimize the loss of lean body mass. Protein is used as an energy source when calories are limited; however, the opposite is not true. Giving excess calories will not lead to increased protein synthesis or retention, but rather lead to overfeeding.

Supplying supranormal doses of protein does not reduce the catabolism of endogenous protein stores, but it does facilitate protein synthesis and reduces negative nitrogen balance [60]. Currently, protein requirements are estimated as 1.5–2.0 g/kg/day for burned adults and 2.5–4.0 g/kg/day for burned children. Non-protein calorie to nitrogen ratio should be maintained between 150:1 for smaller burns and 100:1 for larger burns [61]. Even at these high rates of replacement, most burn patients will experience some loss of muscle protein due to the hormonal and proinflammatory response to burn injury.

Several amino acids are important and play unique roles in recovery after burn. Skeletal muscle and organ efflux of glutamine, alanine, and arginine are increased after burn. These amino acids are important for transport and help supply energy to the liver and healing wounds [62]. Glutamine directly provides fuel for lymphocytes and enterocytes and is essential for maintaining small bowel integrity and preserving gut-associated immune function [63, 64]. Glutamine also provides some level of cellular protection after stress, as it increases the production of heat shock proteins and it is a precursor of glutathione, a critical antioxidant [64–66]. Glutamine is rapidly exhausted from muscle and serum after burn injury, and administration of 25 g/kg/day of glutamine has been found to reduce mortality and length of hospitalization in burn patients [67, 68]. Arginine is another important amino acid because it stimulates T lymphocytes, augments natural killer cell performance, and accelerates nitric oxide synthesis, which improves resistance to infection [69, 70]. The supplementation of arginine in burn patients has led to improvement in wound healing and immune responsiveness [70–72]. Despite some promising results in the burn population, data from critically ill nonburn patients suggest that arginine could potentially be harmful [73]. The current data is insufficient to definitively recommend its use, and further study is warranted.

Vitamins and trace elements

The metabolism of numerous "micronutrients" (vitamins and trace elements) is beneficial after burn as they are important in immunity and wound healing. Severe burn leads to an intense oxidative stress, which combined with the substantial inflammatory response, adds to the depletion of the endogenous antioxidant defenses, which are highly dependent on micronutrients [74, 75]. Decreased levels of vitamins A, C, and D and Fe, Cu, Se, and Zn have been found to negatively impact wound healing and skeletal and immune function [76–78]. Vitamin A decreases time of wound healing via increased epithelial growth, and vitamin C aids collagen creation and cross-linking [79]. Vitamin D contributes to bone density and is deficient after burn, but its exact role and optimal dose after severe burn remains unclear. Pediatric burn patients can suffer significant dysfunction of their calcium and vitamin D homeostasis for a number of reasons. Children with severe burn have increased bone resorption, osteoblast apoptosis, and urinary calcium wasting. Additionally, burned skin is not able to manufacture normal quantities of vitamin D3 leading to further derangements in calcium and vitamin D levels. A study of pediatric burn patients found that supplementation with a multivitamin containing 400 IU of vitamin D2 did not correct vitamin D insufficiency [80–82]. More investigation into therapies to combat calcium and vitamin D deficiency is needed. The trace elements Fe, Cu, Se, and Zn are important for cellular and humoral immunity, but they are lost in large quantities with the exudative burn wound losses [77]. Zn is critical for wound healing, lymphocyte function, DNA replication, and protein synthesis [83]. Fe acts as a cofactor for oxygen-carrying proteins, and Se boosts cell-mediated immunity [75, 84]. Cu is crucial for wound healing and collagen synthesis, and Cu deficiency has been impli- cated in arrhythmias, decreased immunity, and worse outcomes after burn [85]. Replacement of these micro- nutrients has been shown to improve the morbidity of severely burned patients (Table 2) [2, 75, 86, 87].

Routes of nutrition: parenteral vs. enteral

PN was routinely used for burn patients in the 1960s and 1970s, but it has been almost completely replaced by EN [88]. Studies found that PN, alone or in conjunction with EN, is associated with overfeeding, liver dysfunction, decreased immune response, and three-fold increased mortality [89, 90]. PN also appears to increase the secretion of proinflammatory mediators, including TNF, and also can aggravate fatty infiltration of the liver [91, 92]. In addition to these issues, PN has more mechanical and infectious complications of catheters, and PN solutions are significantly more expensive than EN formulas.

EN, in addition to being a safe and cost effective feeding route, has been found to have many advantages. The presence of nutrients within the lumen of the bowel promotes function of the intestinal cells, preserves mucosal architecture and function, stimulates blood supply, decreases bacterial translocation, and improves gut-associated immune function [36, 39]. EN decreases hyperglycemia and hyperosmolarity as it has a "first- pass" hepatic delivery of nutrients [17]. For all of these reasons, EN is the route of choice for severely burned patients. EN can be administered as either gastric or post-pyloric feedings, and both are widely used. Gastric feeding has the advantages of larger diameter tubes, which have less clogging and the ability to give bolus feeds; however, the stomach often develops ileus in the postburn state. Smaller post-pyloric tubes are more prone to clogging and malposition, but they are often more comfortable and post-pyloric feedings can be safely

Table 2 Vitamin and trace element requirements [125]

Age, years	Vitamin A, IU	Vitamin D, IU	Vitamin E, IU	Vitamin C, IU	Vitamin K, mcg	Folate, mcg	Cu, mg	Fe, mg	Se, mcg	Zn, mg
0–13										
Nonburned	1300–2000	600	6–16	15–50	2–60	65–300	0.2–0.7	0.3–8	15–40	2–8
Burned	2500–5000			250–500		1000[a]	0.8–2.8		60–140	12.5–25
≥13										
Nonburned	200–3000	600	23	75–90	75–120	300–400	0.9	8–18	40–60	8–11
Burned	10,000			1000		1000[a]	4		300–500	25–40

[a] Administered three times weekly

continued even during surgical procedures to sustain caloric goals without an increased risk of aspiration [93]. Despite the strong preference to give nutritional support primarily via the gastrointestinal tract, PN can be used in burned patients in whom EN is contraindicated. Further research is warranted regarding if parenteral supplementation of specific dietary components, such as amino acids alone, would be beneficial. PN and EN are usually given in a continuous fashion.

Formulas

The earliest formulas for burn patients consisted of milk and eggs, and although these simple mixtures were relatively successful at providing adequate nutrition, they were very high in fat. Numerous commercially prepared enteral formulas have been developed since that time, all with differing amounts of carbohydrates, protein, fats, and micronutrients (Table 3). Glucose is the preferred energy source for burn patients and they should therefore be administered a high-carbohydrate diet [47, 94]. Parenteral formulas usually consist of 25% dextrose, 5% crystalline amino acids, and maintenance electrolytes. This is often supplemented with infusions of 250 mL of 20% lipid emulsions three times a week to meet essential fatty acid needs [95, 96].

Immune-enhancing diets, or immunonutrition, are nutritional formulas that have been enriched with micronutrients in an effort to improve immune function and wound healing. These formulas gained attention after Gottschlich et al. found that severely burned children given a tube feeding formula containing omega-3 fatty acid, arginine, histidine, and vitamins A and C had significantly fewer wound infections, shorter length of stay, and trended toward improved survival compared to children fed commercially available formulas [97]. This led to the commercial production of similar immune-enhancing diets. Subsequent study of these formulas has shown that they lead to an improvement in neutrophil recruitment, respiratory gas exchange, cardiopulmonary function, mechanical ventilation days, and length of stay in some nonburn populations [98, 99]. Studies in patients with sepsis and pneumonia, however, suggest immune-enhancing diets could have a harmful effect [73, 98]. Little research exists regarding immune-enhancing diets in the burn population. A small study by Saffle et al. found no difference in major outcome variables between the immune-enhancing diet, Impact (Nestle HealthCare, Florham Park, NJ), and a high-protein stress formula, Replete (Nestle HealthCare) [100]. It has been theorized that because of the high volume of feedings given to burn patients, they may receive a satisfactory dose of most immune-enhancing nutrients with the use of conventional diets. A multitude of formulas and numerous methods for calculating nutritional needs are used successfully in the burn population, which suggests that no formula or calculation is perfect, but most are adequate to prevent nutritional complications.

The study of nutrition and metabolism in burn patients is difficult to perform in an exacting and precise method because both the pathophysiology of burn injury and the treatment modalities during the course of burn care are very complex. The effects of differing compositions of nutritional support can easily be confounded by variations in treatment modalities and the complicated pathophysiology of individual burn patients at different stages of their treatment course. A single burn unit takes a very long time to gather data from enough patients which could introduce confounders as other treatment methods advance and change. Multi-institutional trials are also difficult, and any difference in treatment protocols among institutions could overshadow effects of differing nutritional support. A wide range of clinical trials on different nutritional regimens are still being carried out and have not reached convincing consensus on optimal nutrition for burn patients. Physiological/biochemical markers need to be developed or used to assess the potential benefits of these nutrients in parallel to the ongoing evidence-based clinical trials.

Obesity

The rate of obesity has rapidly grown over the past 30 years in both the USA and worldwide [101]. Approximately two thirds of the US population are overweight, and one third meet the BMI criteria for obese [102]. In the general population, obesity is clearly linked with multiple health problems including diabetes, cardiovascular

Table 3 Selected adult enteral nutrition formulas [126]

Formula	Kcal/mL	Carbohydrate, g/L (% calories)	Protein, g/L (% calories)	Fat, g/L (% calories)	Comments
Impact	1.0	130 (53)	56 (22)	28 (25)	IED with arginine, glutamine fiber
Crucial	1.5	89 (36)	63 (25)	45 (39)	IED with arginine, hypertonic
Osmolite	1.06	144 (54)	44 (17)	35 (29)	Inexpensive, isotonic
Glucerna	1.0	96 (34)	42 (17)	54 (49)	Low carbohydrate, for diabetic patients
Nepro	1.8	167 (34)	81 (18)	96 (48)	Concentrated, for patients with renal failure

IED immune-enhancing diet

disease, arthritis, and morbidity [103]. Strangely, overweight and moderately obese patients in surgical and medical intensive care units have been found to have a reduced mortality compared to normal weight patents, despite a higher rate of infections and longer length of stay [104, 105]. Data in the burn population are more limited. A study of the National Burn Repository found a higher mortality for patients listed as obese, but the study was limited due to nonstandard data fields in the database, and the term "obese" was not clearly defined [106]. Two small pediatric studies demonstrated longer hospital stays and a greater need for ventilatory support in obese burned children [107, 108].

Obesity has significant physiologic effects, and fat plays an active role in metabolic regulation. Obesity is associated with an elevated secretion of proinflammatory cytokines, including IL-6, TNF-alpha, and C-reactive protein, and obesity is posited to be a state of chronic inflammation [109, 110]. After burn, obese patients may respond with amplified inflammation, increased hy- permetabolism, brisker and more severe muscle wasting, and severe insulin resistance [111]. Obese patients also have decreased bioavailability of vitamin D3 compared to non-obese patients which can potentially worsen vitamin D and calcium deficiency after burn in this population [80].

Obesity also makes initial nutritional assessment difficult as obese patients can still be malnourished, and using actual body weight in predictive formulas overesti- mates energy needs, while ideal body weight underesti- mates the needs. A few formulas specifically for obese patients have been created but have not been validated. Some clinicians endorse the use of hypocaloric feeding which consists of low-calorie, high-protein diets with the goal of maintaining lean body mass while promoting weight loss and glycemic control [112]. A few small trials in nonburn patients found that patients on a hypocaloric diet had reduced mortality, ventilator dependence, and length of stay [113, 114]. Data remain very limited in nonburn patients and nonexistent in the burn popula- tion, and more studies will need to be done before this can be recommended.

Monitoring of nutritional support

It is challenging to objectively assess the success of nutritional support of a burn patient, as the true endpoint of therapy is global and cannot be measured by one vari- able. The overall goal of therapy is to reestablish normal body composition and metabolic equilibrium, and com- monly measured variables include body weight, nitrogen balance, imaging of lean body mass, and measurement of serum proteins. Functional measures such as exercise tolerance have also been proposed as a possible metric.

Body weight is a tempting measure of nutritional sta- tus as it is easy to obtain and is useful in the general population; however, it can be very misleading in burn patients. The initial fluid resuscitation after severe burn routinely adds 10–20 kg or more of body weight, and al- though this will eventually lead to diuresis, the time course is unpredictable [115]. Additional fluid shifts occur with infections, ventilator support, and hypo- proteinemia, making body weight a very unreliable gauge of nutrition in this population. Patients can have increased total body water for weeks after the burn, which can mask the loss of lean body mass that has certainly occurred [116]. A study of severely burned children found that increasing caloric intake to maintain weight resulted in increased fat mass in- stead of improved lean body mass [48]. Long-term trends are valuable, and weight should be monitored, especially during the rehabilitation phase.

Providing adequate protein intake is an extremely important part of nutritional support after burn. Nitrogen is a fundamental component of amino acids, and as such, the measurement of nitrogen inputs and losses can be used to study protein metabolism. A positive nitrogen balance is associated with periods of growth as it repre- sents an increase in the total body amount of protein, while negative nitrogen balance occurs with burns, trauma, and periods of fasting. Measurement requires accurate urine collection for determination of urea ni- trogen (UUN) as well as documentation of dietary nitro- gen intake [117]. Nitrogen balance for burn patients can be approximated with the following formula:

Nitrogen balance

¼ Nitrogen intake in 24 h −½1:25 × ðUUN þ 4Þ]

Errors in the calculation can come from the two constants. To approximate total urinary nitrogen, 4 g/dL is added to UUN, but total urinary nitrogen may surpass this value in burn patients, leading to an underestimation of nitrogen loss [118, 119]. To account for substantial loss of protein-rich exudates from burn wounds, estimated total urinary nitrogen is multiplied by 1.25, which can similarly underestimate nitrogen losses.

Measurement of serum proteins such as albumin and prealbumin can be utilized to assess nutritional status, but they also have limitations. Metabolic pathways are shifted away from maintenance of these proteins after burn injury, and serum albumin levels are depressed both acutely and chronically, even with successful nu- trition, making it a poor marker [120]. Prealbumin has a short half-life of 2 days which theoretically makes it more responsive to nutritional changes. In reality, the level of prealbumin falls quickly after burn and recovers slowly and may not correlate well with ongoing nutritional status [121]. Protein markers, similar to body weight, should be interpreted in context with the patient's clinical status and with the overall trend in mind.

A few imaging techniques are now available for nutritional monitoring, although due to availability and cost they are typically used in research only. Bioimpedance analysis is a method to calculate total body water and the body's fat-free cell mass by measuring the body's resistance to the passage of electrical currents, although it is unknown how the fluid shifts after burn affects this measurement. Another imaging option is dual x-ray absorptiometry (DEXA) scanning, which can measure bone density and lean body mass.

Graves et al. surveyed 65 burn centers in 2007 regarding their nutritional monitoring practices, and the most commonly used parameters were prealbumin (86% of centers), body weight (75%), calorie count (69%), serum albumin (45.8%), nitrogen balance (54%), and transferrin (16%) [122]. No individual method is universally reliable or applicable for the nutritional monitoring of burn patients, and the overall clinical picture must be incorporated into the assessment.

Overfeeding

The estimation of the nutritional needs of burn patients can be very difficult, and aggressive nutrition in the early post-injury stage can lead to inadvertent overfeeding as the metabolic rate slows and intestinal absorption im- proves. Overfeeding carries numerous complications, in- cluding difficulty weaning from ventilatory support, fatty liver, azotemia, and hyperglycemia. Overfeeding of carbohydrates leads to fat synthesis, increased carbon dioxide, and an increase in the RQ, which worsens respiratory status and makes liberation from the ventila- tor more challenging [44]. After burn, the hypermeta- bolic response leads to the mobilization of all available substrates, and this marked increase of peripheral lipoly- sis can lead to the development of a fatty liver. Over- feeding, via the parenteral or enteral route, can exacerbate the deposition of fat in the liver parenchyma, and fatty liver has been associated with immune dys- function and increased mortality [92]. Azotemia can occur due to the large amounts of protein administered to burn patients. This is important as the massive fluid shifts after burn can cause a prerenal kidney injury, and increased blood urea nitrogen can aggravate the stress already placed on the kidney. Patients with azotemia which does not respond to hydration may need a re- duced amount of protein in their nutrition and need to be closely monitored for signs of renal failure. Nutri- tional support should be continued in patients with renal failure, but blood chemistries should be checked regularly as metabolic derangements are common and must be addressed.

The predictive formulas of nutritional needs should be used as guidelines, and patients' energy requirements should be regularly reassessed. As the acute hypermetabolic phase tapers, the more standard equations and injury/activity factors can be used to avoid overfeeding. Factors such as the changing amount of open wound and physical/occupational therapy activity should be taken into account when estimating nutritional needs.

Nutrition after discharge

It is important that patients continue to receive adequate nutrition after discharge from the hospital, but data on the optimal diet after the acute postburn phase are virtually nonexistent. Because the hypermetabolic state can persist for over a year after burn injury, increased caloric intake with a high protein component is usually recommended for about a year after discharge. Resistance exercise is also recommended to combat continued loss of muscle mass. Patients should regularly weigh themselves to ensure they are maintaining their weight as instructed by the physician and dietician. Oxandrolone is often continued in the outpatient setting, but no data exist regarding the optimum duration of therapy and further study is needed. Nutritional assessments should be a consistent component of outpatient follow-up for burn patients.

Conclusions

The delivery of nutritional support is a vital element of burn care, and the main goal is simply to avoid nutri- tional complications. Effective assessment and manage- ment can optimize wound healing and decrease complications and mortality. EN with high-carbohydrate formulas is beneficial, although nutritional support must be individualized, monitored, and adjusted throughout recovery. Accurate nutritional endpoints and goals need to be established and validated before the optimal nutri- tional regimen can be determined. Basic science analysis of the metabolic changes after burn must be coupled with randomized prospective clinical trials to ascertain the ideal nutritional support for the burn patient.

Abbreviations

ATP: Adenosine triphosphate; EN: Enteral nutrition; IC: Indirect calorimetry; IL: Interleukin; PN: Parenteral nutrition; REE: Resting energy expenditure; rHGH: Recombinant human growth hormone; RQ: Respiratory quotient; TBSA: Total body surface area; TNF: Tumor necrosis factor; UCP1: Uncoupling protein 1; UUN: Urea nitrogen

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References

1. Dickerson RN, Gervasio JM, Riley ML, Murrell JE, Hickerson WL, Kudsk KA, et al. Accuracy of predictive methods to estimate resting energy expenditure of thermally-injured patients. J Parenter Enteral Nutr. 2002;26(1):17–29.
2. Rousseau A-F, Losser M-R, Ichai C, Berger MM. ESPEN endorsed recommendations: nutritional therapy in major burns. Clin Nutr. 2013; 32(4):497–502.
3. Suri MP, Dhingra VJS, Raibagkar SC, Mehta DR. Nutrition in burns: need for an aggressive dynamic approach. Burns. 2006;32(7):880–4.
4. Cuthbertson DP, Angeles Valero Zanuy MA, Leon Sanz ML. Post-shock metabolic response. 1942. Nutr Hosp. 2001;16(5):176-182; discussion 175-176.
5. Porter C, Tompkins RG, Finnerty CC, Sidossis LS, Suman OE, Herndon DN. The metabolic stress response to burn trauma: current understanding and therapies. Lancet. 2016;388(10052):1417–26.
6. Hart DW, Wolf SE, Mlcak R, Chinkes DL, Ramzy PI, Obeng MK, et al. Persistence of muscle catabolism after severe burn. Surgery. 2000; 128(2):312–9.
7. Porter C, Herndon DN, Børsheim E, Bhattarai N, Chao T, Reidy PT, et al. Long-term skeletal muscle mitochondrial dysfunction is associated with hypermetabolism in severely burned children. J Burn Care Res. 2016; 37(1):53–63.
8. Yu YM, Tompkins RG, Ryan CM, Young VR. The metabolic basis of the increase in energy expenditure in severely burned patients. J Parenter Enteral Nutr. 1999;23(3):160–8.
9. Sidossis LS, Porter C, Saraf MK, Børsheim E, Radhakrishnan RS, Chao T, et al. Browning of subcutaneous white adipose tissue in humans after severe adrenergic stress. Cell Metab. 2015;22(2):219–27.
10. Patsouris D, Qi P, Abdullahi A, Stanojcic M, Chen P, Parousis A, et al. Burn induces browning of the subcutaneous white adipose tissue in mice and humans. Cell Rep. 2015;13(8):1538–44.
11. Williams FN, Herndon DN, Jeschke MG. The hypermetabolic response to burn injury and interventions to modify this response. Clin Plast Surg. 2009; 36(4):583–96.
12. Jeschke MG, Finnerty CC, Suman OE, Kulp G, Mlcak RP, Herndon DN. The effect of oxandrolone on the endocrinologic, inflammatory, and hypermetabolic responses during the acute phase postburn. Ann Surg. 2007;246(3):351–2.
13. Demling RH, Seigne P. Metabolic management of patients with severe burns. World J Surg. 2000;24(6):673–80.
14. Jeschke MG, Gauglitz GG, Kulp GA, Finnerty CC, Williams FN, Kraft R, et al. Long-term persistance of the pathophysiologic response to severe burn injury. PLoS One. 2011;6(7):e21245.
15. Przkora R, Barrow RE, Jeschke MG, Suman OE, Celis M, Sanford AP, et al. Body composition changes with time in pediatric burn patients. J Trauma. 2006;60(5):968–71. discussion 971.
16. Chao T, Herndon DN, Porter C, Chondronikola M, Chaidemenou A, Abdelrahman DR, et al. Skeletal muscle protein breakdown remains elevated in pediatric burn survivors up to one-year post-injury. Shock. 2015; 44(5):397–401.
17. Mochizuki H, Trocki O, Dominioni L, Brackett KA, Joffe SN, Alexander JW. Mechanism of prevention of postburn hypermetabolism and catabolism by early enteral feeding. Ann Surg. 1984;200(3):297–310.

18. Peck MD, Kessler M, Cairns BA, Chang Y-H, Ivanova A, Schooler W. Early enteral nutrition does not decrease hypermetabolism associated with burn injury. J Trauma. 2004;57(6):1143–9.
19. Hart DW, Wolf SE, Chinkes DL, Beauford RB, Mlcak RP, Heggers JP, et al. Effects of early excision and aggressive enteral feeding on hypermetabolism, catabolism, and sepsis after severe burn. J Trauma. 2003; 54(4):755–61. discussion 761-754.
20. Chang DW, DeSanti L, Demling RH. Anticatabolic and anabolic strategies in critical illness: a review of current treatment modalities. Shock. 1998;10(3):155–60.
21. Mosier MJ, Pham TN, Klein MB, Gibran NS, Arnoldo BD, Gamelli RL, et al. Early enteral nutrition in burns: compliance with guidelines and associated outcomes in a multicenter study. J Burn Care Res. 2011;32(1):104–9.
22. Peng YZ, Yuan ZQ, Xiao GX. Effects of early enteral feeding on the prevention of enterogenic infection in severely burned patients. Burns. 2001;27(2):145–9.
23. Ong YS, Samuel M, Song C. Meta-analysis of early excision of burns. Burns. 2006;32(2):145–50.
24. Barret JP, Herndon DN. Modulation of inflammatory and catabolic responses in severely burned children by early burn wound excision in the first
24 hours. Arch Surg. 2003;138(2):127–32.
25. Herndon DN, Nguyen TT, Wolfe RR, Maggi SP, Biolo G, Muller M, et al. Lipolysis in burned patients is stimulated by the beta 2-receptor for catecholamines. Arch Surg. 1994;129(12):1301–5.
26. Herndon DN, Hart DW, Wolf SE, Chinkes DL, Wolfe RR. Reversal of catabolism by beta-blockade after severe burns. N Engl J Med. 2001; 345(17):1223–9.
27. Breitenstein E, Chiolero RL, Jequier E, Dayer P, Krupp S, Schutz Y. Effects of beta-blockade on energy metabolism following burns. Burns. 1990; 16(4):259–64.
28. Herndon DN, Rodriguez NA, Diaz EC, Hegde S, Jennings K, Mlcak RP, et al. Long-term propranolol use in severely burned pediatric patients: a randomized controlled study. Ann Surg. 2012;256(3):402–11.
29. Wolf SE, Thomas SJ, Dasu MR, Ferrando AA, Chinkes DL, Wolfe RR, et al. Improved net protein balance, lean mass, and gene expression changes with oxandrolone treatment in the severely burned. Ann Surg. 2003;237(6): 801–10. discussion 810-801.
30. Hart DW, Wolf SE, Ramzy PI, Chinkes DL, Beauford RB, Ferrando AA, et al. Anabolic effects of oxandrolone after severe burn. Ann Surg. 2001; 233(4):556–64.
31. Porro LJ, Herndon DN, Rodriguez NA, Jennings K, Klein GL, Mlcak RP, et al. Five-year outcomes after oxandrolone administration in severely burned children: a randomized clinical trial of safety and efficacy. J Am Coll Surg. 2012;214(4):489–4.
32. Reeves PT, Herndon DN, Tanksley JD, Jennings K, Klein GL, Mlcak RP, et al. Five-year outcomes after long-term oxandrolone administration in severely burned children: a randomized clinical trial. Shock. 2016;45(4):367–74.
33. Branski LK, Herndon DN, Barrow RE, Kulp GA, Klein GL, Suman OE, et al.
Randomized controlled trial to determine the efficacy of long-term growth hormone treatment in severely burned children. Ann Surg. 2009;250(4):514–23.
34. Kim J-B, Cho YS, Jang KU, Joo SY, Choi JS, Seo CH. Effects of sustained release growth hormone treatment during the rehabilitation of adult severe burn survivors. Growth Horm IGF Res. 2016;27:1–6.
35. Takala J, Ruokonen E, Webster NR, Nielsen MS, Zandstra DF, Vundelinckx G, et al. Increased mortality associated with growth hormone treatment in critically ill adults. N Engl J Med. 1999;341(11):785–92.
36. Magnotti LJ, Deitch EA. Burns, bacterial translocation, gut barrier function, and failure. J Burn Care Rehabil. 2005;26(5):383–91.
37. Vicic VK, Radman M, Kovacic V. Early initiation of enteral nutrition improves outcomes in burn disease. Asia Pac J Clin Nutr. 2013;22(4):543–7.
38. Gottschlich MM, Jenkins ME, Mayes T, Khoury J, Kagan RJ, Warden GD. The 2002 Clinical Research Award. An evaluation of the safety of early vs delayed enteral support and effects on clinical, nutritional, and endocrine outcomes after severe burns. J Burn Care Rehabil. 2002;23(6):401–15.
39. Andel D, Kamolz LP, Donner A, Hoerauf K, Schramm W, Meissl G, et al. Impact of intraoperative duodenal feeding on the oxygen balance of the splanchnic region in severely burned patients. Burns. 2005;31(3):302–5.
40. Hansbrough WB, Hansbrough JF. Success of immediate intragastric feeding of patients with burns. J Burn Care Rehabil. 1993;14(5):512–6.
41. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, Society of Critical Care Medicine; American Society for

Parenteral and Enteral Nutrition, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN). J Parenter Enteral Nutr. 2016;40(2): 159–211.
42. Ireton-Jones CS, Turner Jr WW, Liepa GU, Baxter CR. Equations for the estimation of energy expenditures in patients with burns with special reference to ventilatory status. J Burn Care Rehabil. 1992;13(3):330–3.
43. Curreri PW. Assessing nutritional needs for the burned patient. J Trauma. 1990;30(12 Suppl):S20–3.
44. Saffle JR, Medina E, Raymond J, Westenskow D, Kravitz M, Warden GD. Use of indirect calorimetry in the nutritional management of burned patients. J Trauma. 1985;25(1):32–9.
45. McClave SA, Snider HL. Use of indirect calorimetry in clinical nutrition. Nutr Clin Pract. 1992;7(5):207–21.
46. Graf S, Pichard C, Genton L, Oshima T, Heidegger CP. Energy expenditure in mechanically ventilated patients: the weight of body weight! Clin Nutr. 2015. doi:10.1016/j.clnu.2015.11.007.
47. Hart DW, Wolf SE, Zhang XJ, Chinkes DL, Buffalo MC, Matin SI, et al. Efficacy of a high-carbohydrate diet in catabolic illness. Crit Care Med. 2001;29(7): 1318–24.
48. Hart DW, Wolf SE, Herndon DN, Chinkes DL, Lal SO, Obeng MK, et al. Energy expenditure and caloric balance after burn: increased feeding leads to fat rather than lean mass accretion. Ann Surg. 2002;235(1):152–61.
49. Sheridan RL, Yu YM, Prelack K, Young VR, Burke JF, Tompkins RG. Maximal parenteral glucose oxidation in hypermetabolic young children: a stable isotope study. J Parenter Enteral Nutr. 1998;22(4):212–6.
50. Wolfe RR. Maximal parenteral glucose oxidation in hypermetabolic young children. J Parenter Enteral Nutr. 1998;22(4):190.
51. Rodriguez NA, Jeschke MG, Williams FN, Kamolz LP, Herndon DN. Nutrition in burns: Galveston contributions. J Parenter Enteral Nutr. 2011;35(6):704–14.
52. Aarsland A, Chinkes DL, Sakurai Y, Nguyen TT, Herndon DN, Wolfe RR. Insulin therapy in burn patients does not contribute to hepatic triglyceride production. J Clin Invest. 1998;101(10):2233–9.
53. Pierre EJ, Barrow RE, Hawkins HK, Nguyen TT, Sakurai Y, Desai M, et al. Effects of insulin on wound healing. J Trauma. 1998;44(2):342–5.
54. Thomas SJ, Morimoto K, Herndon DN, Ferrando AA, Wolfe RR, Klein GL, et al. The effect of prolonged euglycemic hyperinsulinemia on lean body mass after severe burn. Surgery. 2002;132(2):341–7.
55. Mochizuki H, Trocki O, Dominioni L, Ray MB, Alexander JW. Optimal lipid content for enteral diets following thermal injury. J Parenter Enteral Nutr. 1984;8(6):638–46.
56. Garrel DR, Razi M, Larivière F, Jobin N, Naman N, Emptoz-Bonneton A, et al. Improved clinical status and length of care with low-fat nutrition support in burn patients. J Parenter Enteral Nutr. 1995;19(6):482–91.
57. Alexander JW, Gottschlich MM. Nutritional immunomodulation in burn patients. Crit Care Med. 1990;18(2 Suppl):S149–53.
58. Alexander JW, Saito H, Trocki O, Ogle CK. The importance of lipid type in the diet after burn injury. Ann Surg. 1986;204(1):1–8.
59. Wolfe RR. Metabolic response to burn injury: nutritional implications. Semin Nephrol. 1993;13(4):382–90.
60. Patterson BW, Nguyen T, Pierre E, Herndon DN, Wolfe RR. Urea and protein metabolism in burned children: effect of dietary protein intake. Metabolism. 1997;46(5):573–8.
61. Practice Guidelines Committee ISBI, Subcommittee S, Subcommittee A. ISBI practice guidelines for burn care. Burns. 2016;42(5):953–1021.
62. Soeters PB, van de Poll MC, van Gemert WG, Dejong CH. Amino acid adequacy in pathophysiological states. J Nutr. 2004;134(6 Suppl):1575s–82s.
63. Souba WW. Glutamine: a key substrate for the splanchnic bed. Annu Rev Nutr. 1991;11:285–308.
64. Wischmeyer PE. Can glutamine turn off the motor that drives systemic inflammation? Crit Care Med. 2005;33(5):1175–8.
65. Peng X, Yan H, You Z, Wang P, Wang S. Clinical and protein metabolic efficacy of glutamine granules-supplemented enteral nutrition in severely burned patients. Burns. 2005;31(3):342–6.
66. Garrel D, Patenaude J, Nedelec B, Samson L, Dorais J, Champoux J, et al. Decreased mortality and infectious morbidity in adult burn patients given enteral glutamine supplements: a prospective, controlled, randomized clinical trial. Crit Care Med. 2003;31(10):2444–9.
67. Gore DC, Jahoor F. Glutamine kinetics in burn patients. Comparison with hormonally induced stress in volunteers. Arch Surg. 1994;129(12):1318–23.

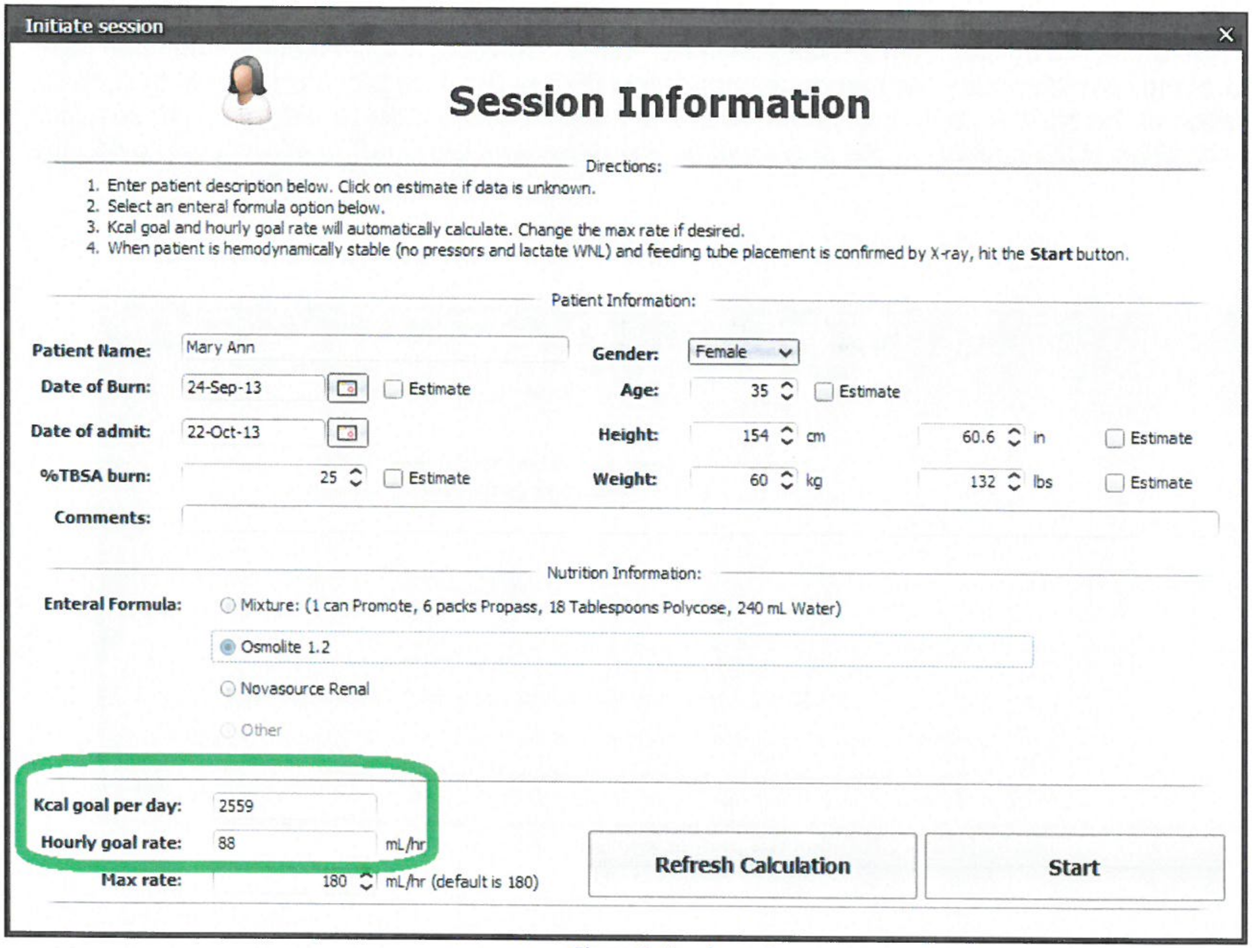
68. Windle EM. Glutamine supplementation in critical illness: evidence, recommendations, and implications for clinical practice in burn care. J Burn Care Res. 2006;27(6):764–72.
69. Yu YM, Ryan CM, Castillo L, Lu XM, Beaumier L, Tompkins RG, et al. Arginine and ornithine kinetics in severely burned patients: increased rate of arginine disposal. Am J Physiol Endocrinol Metab. 2001;280(3):E509–17.
70. Yan H, Peng X, Huang Y, Zhao M, Li F, Wang P. Effects of early enteral arginine supplementation on resuscitation of severe burn patients. Burns. 2007;33(2):179–84.
71. Marin VB, Rodriguez-Osiac L, Schlessinger L, Villegas J, Lopez M, Castillo- Duran C. Controlled study of enteral arginine supplementation in burned children: impact on immunologic and metabolic status. Nutrition. 2006;22(7- 8):705–12.
72. Wibbenmeyer LA, Mitchell MA, Newel IM, Faucher LD, Amelon MJ, Ruffin TO, et al. Effect of a fish oil and arginine-fortified diet in thermally injured patients. J Burn Care Res. 2006;27(5):694–702.
73. Heyland DK, Samis A. Does immunonutrition in patients with sepsis do more harm than good? Intensive Care Med. 2003;29(5):669–71.
74. Gamliel Z, DeBiasse MA, Demling RH. Essential microminerals and their response to burn injury. J Burn Care Rehabil. 1996;17(3):264–72.
75. Berger MM. Antioxidant micronutrients in major trauma and burns: evidence and practice. Nutr Clin Pract. 2006;21(5):438–49.
76. Gottschlich MM, Mayes T, Khoury J, Warden GD. Hypovitaminosis D in acutely injured pediatric burn patients. J Am Diet Assoc. 2004;104(6):931–41. quiz 1031.
77. Berger MM, Shenkin A. Trace element requirements in critically ill burned patients. J Trace Elem Med Biol. 2007;21 Suppl 1:44–8.
78. Berger MM, Binnert C, Chiolero RL, Taylor W, Raffoul W, Cayeux MC, et al. Trace element supplementation after major burns increases burned skin trace element concentrations and modulates local protein metabolism but not whole-body substrate metabolism. Am J Clin Nutr. 2007;85(5):1301–6.
79. Rock CL, Dechert RE, Khilnani R, Parker RS, Rodriguez JL. Carotenoids and antioxidant vitamins in patients after burn injury. J Burn Care Rehabil. 1997; 18(3):269–78. discussion 268.
80. Klein GL. The interaction between burn injury and vitamin D metabolism and consequences for the patient. Curr Clin Pharmacol. 2008;3(3):204–10.
81. Klein GL. Burns: where has all the calcium (and vitamin D) gone? Adv Nutr. 2011;2(6):457–62.
82. Klein GL, Herndon DN, Chen TC, Kulp G, Holick MF. Standard multivitamin supplementation does not improve vitamin D insufficiency after burns. J Bone Miner Metab. 2009;27(4):502–6.
83. Selmanpakoglu AN, Cetin C, Sayal A, Isimer A. Trace element (Al, Se, Zn, Cu) levels in serum, urine and tissues of burn patients. Burns. 1994;20(2):99–103.
84. Hunt DR, Lane HW, Beesinger D, Gallagher K, Halligan R, Johnston D, et al. Selenium depletion in burn patients. J Parenter Enteral Nutr. 1984; 8(6):695–9.
85. Sampson B, Constantinescu MA, Chandarana I, Cussons PD. Severe hypocupraemia in a patient with extensive burn injuries. Ann Clin Biochem. 1996;33(Pt 5):462–4.
86. Meyer NA, Muller MJ, Herndon DN. Nutrient support of the healing wound. New Horiz. 1994;2(2):202–14.
87. Berger MM, Baines M, Raffoul W, Benathan M, Chiolero RL, Reeves C, et al. Trace element supplementation after major burns modulates antioxidant status and clinical course by way of increased tissue trace element concentrations. Am J Clin Nutr. 2007;85(5):1293–300.
88. Ireton-Jones CS, Baxter CR. Nutrition for adult burn patients: a review. Nutr Clin Pract. 1991;6(1):3–7.
89. Herndon DN, Barrow RE, Stein M, Linares H, Rutan TC, Rutan R, et al. Increased mortality with intravenous supplemental feeding in severely burned patients. J Burn Care Rehabil. 1989;10(4):309–13.
90. Herndon DN, Stein MD, Rutan TC, Abston S, Linares H. Failure of TPN supplementation to improve liver function, immunity, and mortality in thermally injured patients. J Trauma. 1987;27(2):195–204.
91. Fong YM, Marano MA, Barber A, He W, Moldawer LL, Bushman ED, et al. Total parenteral nutrition and bowel rest modify the metabolic response to endotoxin in humans. Ann Surg. 1989;210(4):449–56. discussion 456-447.
92. Barret JP, Jeschke MG, Herndon DN. Fatty infiltration of the liver in severely burned pediatric patients: autopsy findings and clinical implications. J Trauma. 2001;51(4):736–9.
93. Jenkins ME, Gottschlich MM, Warden GD. Enteral feeding during operative procedures in thermal injuries. J Burn Care Rehabil. 1994;15(2):199–205.

94. Boulétreau P, Chassard D, Allaouchiche B, Dumont JC, Auboyer C, Bertin- Maghit M, et al. Glucose-lipid ratio is a determinant of nitrogen balance during total parenteral nutrition in critically ill patients: a prospective, randomized, multicenter blind trial with an intention-to-treat analysis. Intensive Care Med. 2005;31(10):1394–400.
95. Berger M. Basics in clinical nutrition: nutritional support in burn patients. E Spen Eur E J Clin Nutr Metab. 2009;4(6):e308–12.
96. Chen Z, Wang S, Yu B, Li A. A comparison study between early enteral nutrition and parenteral nutrition in severe burn patients. Burns. 2007; 33(6):708–12.
97. Gottschlich MM, Jenkins M, Warden GD, Baumer T, Havens P, Snook JT, et al. Differential effects of three enteral dietary regimens on selected outcome variables in burn patients. J Parenter Enteral Nutr. 1990;14(3):225–36.
98. Heys SD, Walker LG, Smith I, Eremin O. Enteral nutritional supplementation with key nutrients in patients with critical illness and cancer: a meta-analysis of randomized controlled clinical trials. Ann Surg. 1999;229(4):467–77.
99. Bower RH, Cerra FB, Bershadsky B, Licari JJ, Hoyt DB, Jensen GL, et al. Early enteral administration of a formula (Impact) supplemented with arginine, nucleotides, and fish oil in intensive care unit patients: results of a multicenter, prospective, randomized, clinical trial. Crit Care Med. 1995;23(3):436–49.
100. Saffle JR, Wiebke G, Jennings K, Morris SE, Barton RG. Randomized trial of immune-enhancing enteral nutrition in burn patients. J Trauma. 1997;42(5):793–2.
101. Pak TY, Ferreira S, Colson G. Measuring and tracking obesity inequality in the United States: evidence from NHANES, 1971-2014. Popul Health Metr. 2016;14(1):12.
102. Flegal KM, Kruszon-Moran D, Carroll MD, Fryar CD, Ogden CL. Trends in obesity among adults in the United States, 2005 to 2014. JAMA. 2016; 315(21):2284–91.
103. Malnick SD, Knobler H. The medical complications of obesity. QJM. 2006; 99(9):565–79.
104. Akinnusi ME, Pineda LA, El Solh AA. Effect of obesity on intensive care morbidity and mortality: a meta-analysis. Crit Care Med. 2008;36(1):151–8.
105. Mullen JT, Moorman DW, Davenport DL. The obesity paradox: body mass index and outcomes in patients undergoing nonbariatric general surgery. Ann Surg. 2009;250(1):166–72.
106. Carpenter AM, Hollett LP, Jeng JC, Wu J, Turner DG, Jordan MH. How long a shadow does epidemic obesity cast in the burn unit? A dietitian's analysis of the strengths and weaknesses of the available data in the National Burn Repository. J Burn Care Res. 2008;29(1):97–101.
107. Gottschlich MM, Mayes T, Khoury JC, Warden GD. Significance of obesity on nutritional, immunologic, hormonal, and clinical outcome parameters in burns. J Am Diet Assoc. 1993;93(11):1261–8.
108. Patel L, Cowden JD, Dowd D, Hampl S, Felich N. Obesity: influence on length of hospital stay for the pediatric burn patient. J Burn Care Res. 2010; 31(2):251–6.
109. McClave SA, Frazier TH, Hurt RT, Kiraly L, Martindale RG. Obesity, inflammation, and pharmaconutrition in critical illness. Nutrition. 2014;30(4):492–4.
110. Cave MC, Hurt RT, Frazier TH, Matheson PJ, Garrison RN, McClain CJ, et al. Obesity, inflammation, and the potential application of pharmaconutrition. Nutr Clin Pract. 2008;23(1):16–34.
111. Jeevanandam M, Young DH, Schiller WR. Obesity and the metabolic response to severe multiple trauma in man. J Clin Invest. 1991;87(1):262–9.
112. Berger MM, Chiolero RL. Hypocaloric feeding: pros and cons. Curr Opin Crit Care. 2007;13(2):180–6.
113. Dickerson RN, Boschert KJ, Kudsk KA, Brown RO. Hypocaloric enteral tube feeding in critically ill obese patients. Nutrition. 2002;18(3):241–6.
114. McCowen KC, Friel C, Sternberg J, Chan S, Forse RA, Burke PA, et al. Hypocaloric total parenteral nutrition: effectiveness in prevention of hyperglycemia and infectious complications—a randomized clinical trial. Crit Care Med. 2000;28(11):3606–11.
115. Gump FE, Kinney JM. Energy balance and weight loss in burned patients. Arch Surg. 1971;103(4):442–8.
116. Zdolsek HJ, Lindahl OA, Angquist KA, Sjoberg F. Non-invasive assessment of intercompartmental fluid shifts in burn victims. Burns. 1998;24(3):233–40.
117. Graves C, Saffle J, Morris S. Comparison of urine urea nitrogen collection times in critically ill patients. Nutr Clin Pract. 2005;20(2):271–5.
118. Konstantinides FN, Radmer WJ, Becker WK, Herman VK, Warren WE, Solem LD, et al. Inaccuracy of nitrogen balance determinations in thermal injury with calculated total urinary nitrogen. J Burn Care Rehabil. 1992;13(2 Pt 1):254–60.

Appendix 1

Description of the Nutrition Decision Support System

The Nutrition Decision Support System software offers the user a nutrition recommendation based on individual patient data entered into the system by the bedside provider. Upon starting the application, the user is prompted to provide patient information as well as the enteral formula that will be used to feed the patient (Figure 1). Based on this information the system computes a caloric goal per day for that patient as well as the hourly rate required to reach that goal.



Initiate session

Session Information

Directions:

1. Enter patient description below. Click on estimate if data is unknown.
2. Select an enteral formula option below.
3. Kcal goal and hourly goal rate will automatically calculate. Change the max rate if desired.
4. When patient is hemodynamically stable (no pressors and lactate WNL) and feeding tube placement is confirmed by X-ray, hit the **Start** button.

Patient Information:

Patient Name: Mary Ann
Gender: Female
Date of Burn: 24-Sep-13 ☐ Estimate
Age: 35 ☐ Estimate
Date of admit: 22-Oct-13
Height: 154 cm 60.6 in ☐ Estimate
%TBSA burn: 25 ☐ Estimate
Weight: 60 kg 132 lbs ☐ Estimate
Comments:

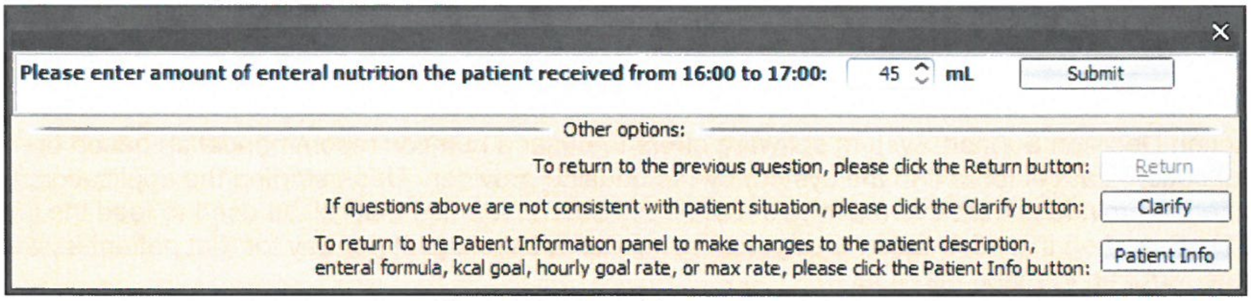
Nutrition Information:

Enteral Formula:
○ Mixture: (1 can Promote, 6 packs Propass, 18 Tablespoons Polycose, 240 mL Water)
● Osmolite 1.2
○ Novasource Renal
○ Other

Kcal goal per day: 2559
Hourly goal rate: 88 mL/hr
Max rate: 180 mL/hr (default is 180)

Figure 1: Session setup screen

Once the nutrition session starts, the Nutrition DSS will prompt the user each hour to enter how much enteral nutrition the patient received during the previous hour (Figure 2).



Please enter amount of enteral nutrition the patient received from 16:00 to 17:00: 45 mL

Other options:

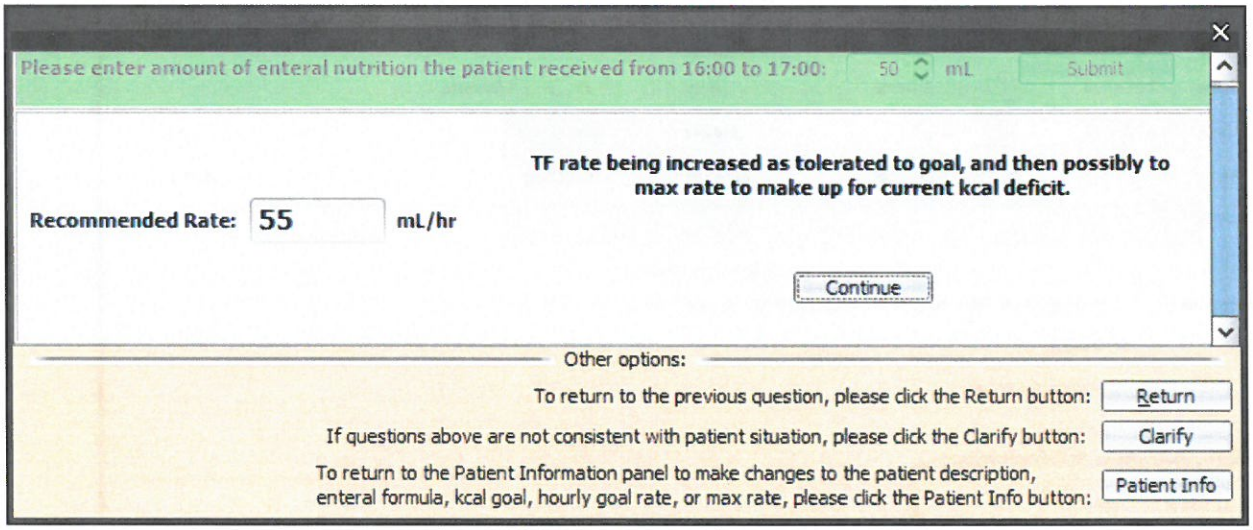
To return to the previous question, please click the Return button:

If questions above are not consistent with patient situation, please click the Clarify button:

To return to the Patient Information panel to make changes to the patient description, enteral formula, kcal goal, hourly goal rate, or max rate, please click the Patient Info button:

Figure 2: Hourly nutrition rate prompt

Based on this information, the system then provides the user with a new recommended enteral nutrition rate for the next hour along with the reason for that recommendation (Figure 3). This process repeats itself every hour for the duration of the session, with the system utilizing a mathematical model (*at this point not specific to the physiologic condition of the patient, as the only input is how much was received*) to attempt to provide the caloric goal.



Please enter amount of enteral nutrition the patient received from 16:00 to 17:00: 50 mL

TF rate being increased as tolerated to goal, and then possibly to max rate to make up for current kcal deficit.

Recommended Rate: 55 mL/hr

Other options:

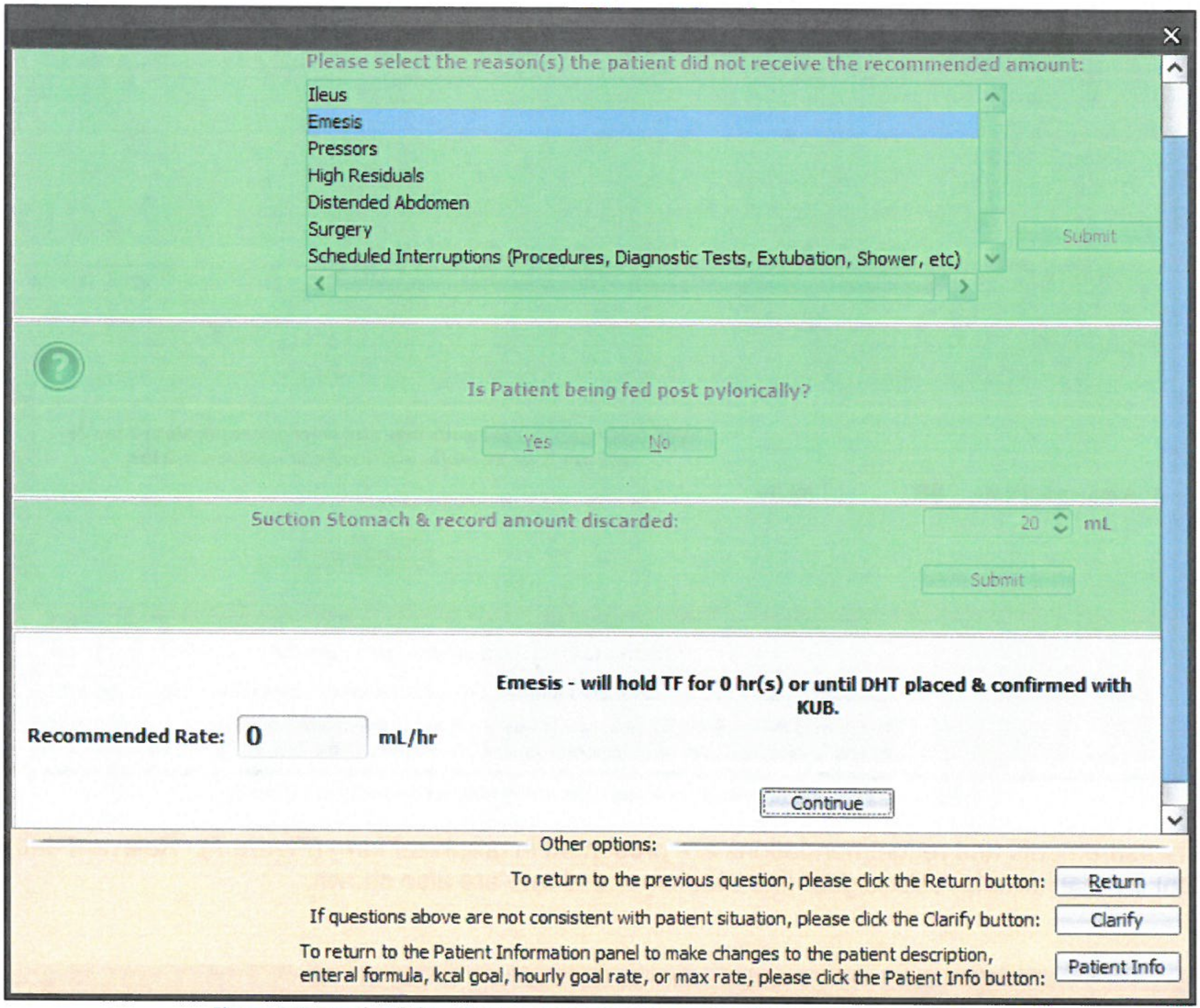
To return to the previous question, please click the Return button:

If questions above are not consistent with patient situation, please click the Clarify button:

To return to the Patient Information panel to make changes to the patient description, enteral formula, kcal goal, hourly goal rate, or max rate, please click the Patient Info button:

Figure 3: Hourly nutrition rate prompt with new recommendation

If at some point, however, the user indicates that the recommendation provided by the system was not followed, the system will prompt the user for a reason and, based on that answer, it will ask questions to assess the perceived status of the patient based upon the judgment of the provider, and then provide new instructions and recommendations (Figure 4).



Please select the reason(s) the patient did not receive the recommended amount:

- Ileus
- Emesis
- Pressors
- High Residuals
- Distended Abdomen
- Surgery
- Scheduled Interruptions (Procedures, Diagnostic Tests, Extubation, Shower, etc)

Is Patient being fed post pylorically?

Suction Stomach & record amount discarded: 20 mL

Emesis - will hold TF for 0 hr(s) or until DHT placed & confirmed with KUB.

Recommended Rate: 0 mL/hr

Other options:

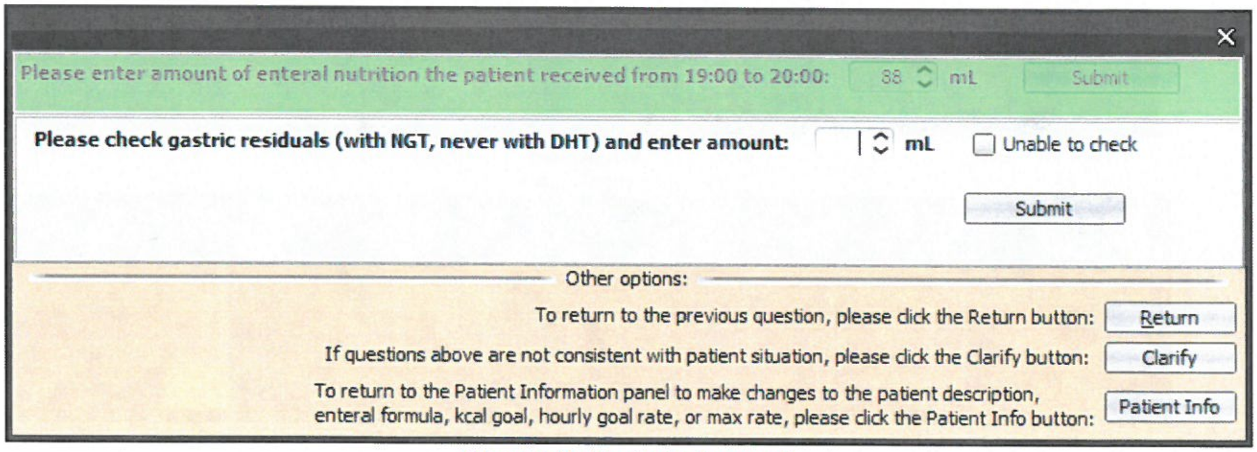
To return to the previous question, please click the Return button:

If questions above are not consistent with patient situation, please click the Clarify button:

To return to the Patient Information panel to make changes to the patient description, enteral formula, kcal goal, hourly goal rate, or max rate, please click the Patient Info button:

Figure 4: Example of the situation assessment prompt with new recommendation

In addition to prompting the user every hour for the enteral rate, every 4 hours the system will also ask the user to measure gastric residuals (Figure 5). If the residual volume is found to be higher than preconceived limits (*that have not been tested yet*), the system will then adjust the recommendation provided to account (Figure 6).



Please enter amount of enteral nutrition the patient received from 19:00 to 20:00: 88 mL

Please check gastric residuals (with NGT, never with DHT) and enter amount: mL ☐ Unable to check

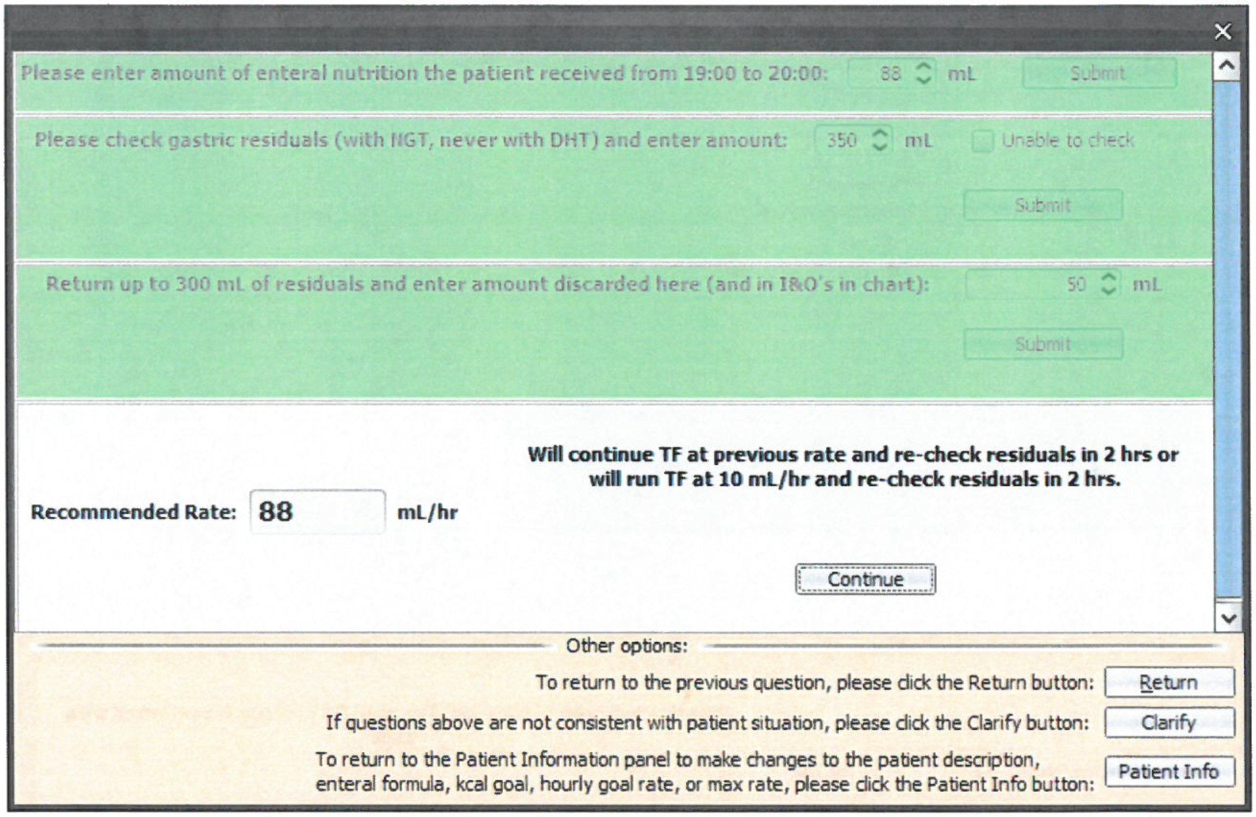
Other options:

To return to the previous question, please click the Return button:

If questions above are not consistent with patient situation, please click the Clarify button:

To return to the Patient Information panel to make changes to the patient description, enteral formula, kcal goal, hourly goal rate, or max rate, please click the Patient Info button:

Figure 5: Residuals check prompt



Please enter amount of enteral nutrition the patient received from 19:00 to 20:00: 88 mL

Please check gastric residuals (with NGT, never with DHT) and enter amount: 350 mL

Return up to 300 mL of residuals and enter amount discarded here (and in I&O's in chart): 50 mL

Will continue TF at previous rate and re-check residuals in 2 hrs or will run TF at 10 mL/hr and re-check residuals in 2 hrs.

Recommended Rate: 88 mL/hr

Other options:

To return to the previous question, please click the Return button:

If questions above are not consistent with patient situation, please click the Clarify button:

To return to the Patient Information panel to make changes to the patient description, enteral formula, kcal goal, hourly goal rate, or max rate, please click the Patient Info button:

Figure 6: Example of instructions and new recommendation for high residuals

All the measurements and recommendations are presented in graphical form (Figure 7). Relevant data such as current enteral formula, caloric goal and recommended rate are also shown.

Shields Power Curve: The Nutrition Decision Support System

M. Ann

Formula: Osmolite 1.2 | **Recommended Rate:** 88 mL/hr | **Time Remaining:** 52:18 | **System Time:** (10) 20:07

Hourly goal rate: 88 mL/hr

Max rate: 180 mL/hr

Daily goal: 2559 Kcal/day

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Figure 7: Main application window with graphical displays