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14. ABSTRACT

The objective of this 300 patient multi-center observational study was to evaluate resuscitation volumes and outcomes of patients admitted to five verified burn centers who underwent fluid resuscitation utilizing the Burn Navigator (BN), a burn resuscitation clinical decision support tool. A total of 285 patients were eligible for analysis. There was no difference among the centers in terms of average age (45.5 + 16.8 years), BMI (29.2 + 6.9), ISS (21.2 + 12.8), or median TBSA (34 [25.8, 47]). Analysis of patients in the first 24 hours of resuscitation revealed average volumes for primary (crystalloid) and total fluids administered of 4.07 ± 1.76 mL/kg/TBSA (or 151.48 ± 77.46 mL/kg), and 4.68 ± 2.06 mL/kg/TBSA (or 175.01 ± 92.22 mL/kg), respectively. Examining patients who presented in a delayed fashion revealed average volumes for primary and total fluids of 5.28 ± 2.54 mL/kg/TBSA (or 201.11 ± 106.53 mL/kg), 6.35 ± 2.95 mL/kg/TBSA (or 244.08 ± 133.5 mL/kg), respectively. There was a decreased incidence of shock in the BN-guided group ($p < 0.05$). The BN provides comparable resuscitation volumes of primary crystalloid fluid to the Parkland Formula, recommends total fluid infusion less than the Ivy Index, and was associated with a decreased incidence of shock. Early initiation of the BN device resulted in lower overall fluid volumes. There was a total of 156 resuscitation-related complications reported across the 5 sites with an average incidence of 44.4 % incidence. For further details, please see attached abstracts and manuscript (pending publication--journal revision stage) listed below. The Burn Navigator appeared to standardize fluid resuscitations across 5 major US burn centers. With primary fluid volumes near the Parkland formula, the device can be utilized effectively in burn centers, and further study should exam the utility of this device in facilities that do not commonly treat burn injuries, as well as the battlefield.

15. SUBJECT TERMS

Burn resuscitation, decision-support

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1. INTRODUCTION:

The goal of this study is to validate the Burn Navigator as an effective decision support tool in acute burn resuscitation by demonstrating that total intravenous fluids infused during resuscitation is an adequate amount to prevent complication associated with dehydration/under-perfusion while avoiding the consequences of giving too much intravenous fluid in the acute phase after burn injury.

2. KEYWORDS:

Burn resuscitation, decision-support

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Objective 1: Describe Burn Navigator resuscitations and build a comprehensive database of Burn Navigator data

Objective 2: Assess resuscitation outcomes from the Burn Navigator and compare burn center differences in resuscitation outcomes.

Objective 3: Harmonize the comprehensive Burn Navigator database with other ABA studies in order to obtain a common dataset to evaluate the efficacy of the Burn Navigator.

Task 1: Prepare regulatory documents and research protocol – core protocol approved by IRB on 31AUG2017

Task 2: Build comprehensive Burn Navigator database (e.g. retrospective and prospective data collection)

Task 3: Analyze Burn Navigator database to assess association between resuscitation volumes and outcomes of interest

What was accomplished under these goals?

1. Core protocol and all participating sites received HRPO closure approvals on 13 Sept 2021.
2. As of 09 July 2021, the following are enrollment numbers and data completion per site:

Site	Retrospective Enrolled	Prospective Enrolled	Unidentified Enrolled
USAISR	50	54	0
Arizona Burn Center	16	42	0
UTMB_Galveston	9	8	0
UTSW_Parkland	1	13	0
Washington_Harborview	35	72	0
Total Enrolled Per Section	**111**	**189**	**0**

Total Enrolled	**300**

REDCap and data management: Total w/complete data:294*

Site	# of Subject Completed Data entered in RedCap	# of Subject Data Incomplete/Queries Pending
USAISR	104	0
Arizona Burn Center	58	0
UTMB_Galveston	11	6
UTSW_Parkland	14	0
Washington_Harborview	107	0

Target required for clinical significance: 300 between 5 sites

Target approved for clinical significance: 300 (between 5 sites)

3. *UTMB—unable to complete data on 6 subjects they enrolled before closing site per institution's research director.

What opportunities for training and professional development has the project provided?

Nothing to report.

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

Nothing to report.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change.

Nothing to report this period that hasn't already been reported in previous reports.

Actual or anticipated problems or delays and actions or plans to resolve them.

Nothing to report this period that hasn't already been reported in previous reports.

Changes that had a significant impact on expenditures.

Nothing to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

Nothing to report.

Significant changes in use or care of vertebrate animals.

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications.

Title
Initial Results of the American Burn Association (ABA) Observational Multi-Center Evaluation on the Effectiveness of the Burn Navigator
Authors
Julie A. Rizzo MD[1,2,#]; Nehemiah T. Liu MS[1]; Elsa C. Coates MSN[1]; Maria L. Serio-Melvin MSN[1]; Kevin N. Foster MD[3]; Misbah Shabbir MS[4]; Tam N. Pham MD[5]; Jose Salinas, PhD[1]
Institution
[1] United States Institute of Surgical Research, Fort Sam Houston TX
[2] Uniformed Services University of Health Sciences, Bethesda MD
[3] Arizona Burn Center Valleywise Health, Phoenix AZ
[4] UT-Southwestern Medical Center, Dallas TX
[5] Harborview Regional Burn Center, Seattle WA
Journal
Journal of Burn Care & Research
Publication
Manuscript accepted and awaiting publication as of 08 Oct 2021

Books or other non-periodical, one-time publications. 997

Nothing to report.

Other publications, conference papers, and presentations.

1. "Initial Results of the American Burn Association (ABA) Observational Multi-Center Evaluation on the Effectiveness of the Burn Navigator"* (podium presentation at 53rd Annual ABA meeting, April 6-9, 2021---virtual conference.

2. "The Battle of the Titans – Comparing Resuscitation Between 5 Major Burn Centers Using the Burn Navigator" (abstract podium presentation acceptance at ABA Southern Regional, November 4-7, 2021, New Orleans, LA.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**.

Nothing to report.

- **Other Products**

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: *Jose Salinas*
Project Role: *Principal Investigator*
Researcher Identifier (e.g. ORCID ID): 0000-0002-6368-6375
Nearest person month worked: *No change*

Contribution to Project: *Responsible for overall conduct of study, study design, data analysis, and preparation of manuscripts*

Name: *Julie Rizzo*
Project Role: *Associate Investigator*
Researcher Identifier (e.g. ORCID ID): 0000-0002-4066-7331
Nearest person month worked: *No Change*
Contribution to Project: *Serve as a resource to the PI, study design, data analysis, and preparation of manuscripts*

Name: *Maria Serio-Melvin*
Project Role: *Associate Investigator*
Researcher Identifier (e.g. ORCID ID): 0000-0001-9084-1222
Nearest person month worked: *No Change*
Contribution to Project: *Serve as a resource to the PI, study design, data analysis, and preparation of manuscripts*

Name: *Elsa Coates*
Project Role: *Clinical Research Coordinator*
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: *No change*
Contribution to Project: *Responsible for daily efficient functioning of study, assist in the preparation of progress reports, and maintaining all regulatory documents*

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report.

What other organizations were involved as partners?

Nothing to report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES:

Evaluation of the Effectiveness of the Burn Navigator in Improving Resuscitation Outcomes

MB150113
W81XWH-16-2-0055

APPENDIX A

PI: Jose Salinas PhD **Org:** USAISR / ABA **Award Amount:** $1,985,800

Study/ Aim

- The goal of this study is to validate the Burn Navigator as an effective decision support tool in acute burn resuscitation by demonstrating that total intravenous fluids infused during resuscitation is an adequate amount to prevent complication associated with dehydration/under-perfusion while avoiding the consequences of giving too much intravenous fluid in the acute phase after burn injury.

Approach

Prospective and retrospective evaluation of patients with burn injury admitted to 5 burn centers that currently use the Burn Navigator technology.

This prospective observational study, with an embedded retrospective component, will provide the latest information on the Burn Navigator as a decision support tool during burn resuscitation.

Timeline and Cost

Activities FY	19	20	21
Approved IRB Protocol			
Patients Enrollment			
Data Analysis/Manuscript preparation			
Proposal Budget ($K)	**$752**	**$431**	**$57**

Updated: OCT 2021

Work completed to date:

- Total 294/300 (98%) with complete data in REDCap.
- All participating sites received IRB/HRPO closer approvals
- 1st manuscript accepted to JBCR---April 2021

FY2021 Goals:

- Complete Final Technical report

Payoff/Deliverables:

- Provide validation of a clinical decision support FDA-approved device to guide burn resuscitation for the military far forward environment.
- Validate use of resuscitation decision support algorithms in various burn environments/centers.

Comments/Challenges/Issues/Concerns (overall)

- A no-cost extension (NCE) approved to extend project to FY 21 and all contract amended with sites are complete.
- COVID-19 restrictions for completing data with some sites.
- UTMB closed before data could be completed in REDCap (6 subjects)

Budget Expenditure to Date

- Budget Expenditure to date is $1,985,794.

Initial Results of the American Burn Association (ABA) Multi-Center Evaluation on the Effectiveness of the Burn Navigator

Introduction

The Burn Navigator (BN) is an FDA-cleared clinical decision support tool used to aid fluid resuscitation after major burn injury. The BN provides users with hourly recommendations for fluid titration during the initial resuscitation based on various factors. The objective of this multi-center observational study was to evaluate the resuscitation volumes and related outcomes of patients admitted to five ABA verified burn centers who underwent intravenous fluid resuscitation utilizing the BN.

Methods

Data was collected from 300 patients who were resuscitated utilizing the BN. Two analyses were performed: examination of the first 24 hours of resuscitation after burn injury and examination of 24 hours of resuscitation using the BN, regardless of when the resuscitation began, to account for patients who presented in a delayed fashion. Patients were classified as having followed the BN device if all hourly fluid rates were within 40 mL of the BN recommendations (20 mL above or below) for that hour at least 75% of the time.

Results

For 285 patients, average age, weight, and TBSA were 45.6 $\pm$ 16.8 years, 87.0 $\pm$ 22.8 kg, and 39.0 $\pm$ 17.8%, with partial/full thickness percentages of 22.2 $\pm$ 15.2% and 17.0 $\pm$ 19.7%, respectively. Analysis of 286 patients in the first 24 hours of resuscitation revealed an average of 4.07 $\pm$ 1.76 mL/kg/TBSA and 151.48 $\pm$ 77.46 mL/kg of primary crystalloid fluid. When considering all fluids administered to include colloids and medications, enteral and oral feeds, and oral resuscitation fluids, average volumes in the first 24 hours were 4.68 $\pm$ 2.06 mL/kg/TBSA and 175.01 $\pm$ 92.22 mL/kg. To account for delayed presentation after burn injury, examining 24 hours of resuscitation regardless of the initiation of resuscitation, average volumes for primary and total fluids were 5.28 $\pm$ 2.54 mL/kg/TBSA, 201.11 $\pm$ 106.53 mL/kg, 6.35 $\pm$ 2.95 mL/kg/TBSA and 244.08 $\pm$ 133.5 mL/kg respectively. There was a significant decrease incidence of shock in the BN-guided group versus the non-BN-guided group ($p< 0.05$).

Conclusions

The Burn Navigator provides comparable resuscitation volumes of primary crystalloid fluid to the Parkland Formula. When all fluids are con sidered, the BN device recommends total fluid infusion less than the Ivy Index (250 mL/kg/24 hrs) and was associated with a decreased incidence of shock. Early

initiation of the BN device resulted in lower overall fluid volumes during the first 24 hours of resuscitation.

Applicability of Research to Practice

The BN navigator has been shown to be comparable to established standards of care. Use of this device is an effective tool for fluid resuscitation in mulitple clinical settings and provides an additional adjunct for clinical staff to use during the management of severely burned patients.

Funding for the study

Department of Defense, Grant (W81XWH-16-2-0055) awarded to the ABA

APPENDIX C

Initial Results of the American Burn Association (ABA) Observational Multi-Center Evaluation on the Effectiveness of the Burn Navigator

ABSTRACT

The objective of this multi-center observational study was to evaluate resuscitation volumes and outcomes of patients who underwent fluid resuscitation utilizing the Burn Navigator (BN), a resuscitation clinical decision support tool. Two analyses were performed: examination of the first 24 hours of resuscitation, and the first 24 hours post-burn regardless of when the resuscitation began, to account for patients who presented in a delayed fashion. Patients were classified as having followed the BN (FBN) if all hourly fluid rates were within ±20 mL of BN recommendations for that hour at least 83% of the time, otherwise they were classified as not having followed BN (NFBN). Analysis of resuscitation volumes for FBN patients in the first 24 hours resulted in average volumes for primary crystalloid) and total fluids administered of 4.07 ± 1.76 mL/kg/TBSA (151.48 ± 77.46 mL/kg), and 4.68 ± 2.06 mL/kg/TBSA (175.01 ± 92.22 mL/kg), respectively. Patients who presented in a delayed fashion revealed average volumes for primary and total fluids of 5.28 ± 2.54 mL/kg/TBSA (201.11 ± 106.53 mL/kg), 6.35 ± 2.95 mL/kg/TBSA (244.08 ± 133.5 mL/kg), respectively. There was a significant decrease in the incidence of burn shock in the FBN group ($p < 0.05$). This study shows that the BN provides comparable resuscitation volumes of primary crystalloid fluid to the Parkland Formula, recommends total fluid infusion less than the Ivy Index, and was associated with a decreased incidence of burn shock. Early initiation of the BN device resulted in lower overall fluid volumes.

Key words: burn resuscitation, decision support tool, Burn Navigator

Introduction

Fluid resuscitation is the cornerstone of initial patient management for large burn injuries. Burns that encompass at least 20% total body surface area (TBSA) generate a systemic response that normally requires active fluid resuscitation to avoid burn shock [1]. This is due to large fluid shifts and third spacing from the intravascular space to other areas of the body in response to the burn leading to reduced organ perfusion. In order to mitigate loss of intravascular volume in these patients, intravenous fluid resuscitation is required to replace ongoing fluid loss during the initial 24 to 48 hours post-burn [2].

Delivery of fluid to the patient after severe burn injury requires a balanced regimen. Excessive fluid administration can lead to life-threatening complications such as abdominal, extremity, or intraocular compartment syndrome. On the other hand, insufficient fluid administration can lead to complications such as acute kidney injury, burn shock, or multi-organ failure. Several burn fluid resuscitation formulas and guidelines have been developed to assist providers with appropriate fluid administration during the resuscitation period. Historical formulas are based on estimates for fluid volume requirements in the first 24 hours post burn of between 2 ml/kg/TBSA for the Modified Brooke Formula and 4 ml/kg/TBSA for the Parkland [3, 4]. Newer guidelines refine these requirements by defining approaches based on hourly titration of the resuscitative fluid to maintain adequate urinary output (UO) while reducing the risk of over-resuscitation and related complications [5]. Site specific formulas for adjusting resuscitative fluid rates based on the hourly UO values are used as the titration approach for maintaining UO values within expected target ranges during the resuscitative period. For these approaches, UO is used as a non-invasive surrogate for cardiac output as an indicator of organ perfusion.

Maintaining optimal hourly resuscitation volumes after burn injury is a complex process when considering all patient parameters. Often, large volumes of isotonic fluid are required as continuous infusions and are coupled with fluid adjuncts, such as colloids and blood products. Documentation of intake and output on flowsheets or in the electronic medical record is helpful, but it does not facilitate easy interpretation of the data for quick and accurate decision-making.

Therefore, to assist providers in making changes to primary crystalloid intravenous fluid rates during an active resuscitation, the United States Army Institute of Surgical Research (USAISR) and University of Texas Medical Branch (UTMB) developed the Burn Resuscitation Decision Support System (BRDSS) [6, 7]. This software application utilizes a mathematical model to estimate fluid volume for the next hour based on the patient's last three UO volumes, last crystalloid fluid infusion volume, burn size, weight, time post-burn, and other variables. The system incorporates a graphical user interface and a set of operational business rules were developed to enhance the safety, usability, and clinical decision support features of the software. Previous studies with the BRDSS showed that overall resuscitation volumes were reduced using the system compared to resuscitations performed manually [7]. The BRDSS was subsequently commercialized as the Burn Navigator™ (BN) System by Arcos Medical and has been used extensively within the DoD and across multiple burn centers. However, no comprehensive studies have examined the performance of the system when used in these different environments.

The objective of this multi-center observational study was to evaluate the resuscitation volumes and related outcomes of patient admitted to five ABA verified burn centers who underwent intravenous fluid resuscitation utilizing the BN. The goal of the project was to validate the performance of the BN as an effective clinical tool when used in different environments and burn

care settings. The hypothesis of this study was that use of the BN across different environments would result in 24 resuscitation volumes comparable to the Parkland Formula of 4 ml/kg/TBSA.

Methods

Study design: The study was implemented as an observational, non-interventional consisting of both retrospective and prospective data collection components across the 5 participating centers with a target goal of 300 patients across all sites.

Setting and participants: The participating sites were 5 American Burn Association-verified burn centers that broadly represent geographic and resuscitation practice differences in the US. Data was collected from both the BN system and electronic medical records (EMR) during routine medical care of burn patients that where the BN was used. Each site investigator obtained Institutional Review Board approval for their site. The STROBE guidelines were used to ensure consistent reporting of all relevant domains for this observational study [8].

Inclusion criteria included adult patients ($\geq$ 18 years old) with a burn injury affecting $\geq$ 20% TBSA, weight $\geq$ 40 kilograms, admitted to one of the five burn centers within 24 hours of their injury and expected to live for at least 24 hours, as well as receiving intravenous fluid resuscitation for their burn injury utilizing the BN. Patients with primary electrical burns were excluded from this study.

Variables and data sources: The extent of the patients' burn injuries were manually estimated by expert burn care providers per their usual clinical practice, by using the Lund–Browder diagram.

Data collected from the EMR included patient demographics, burn characteristics, intake and output volumes, medications, labs, and complications. Intake and output data were also collected from the BN. Fluid data collected from both sources included fluids prior to ICU admission

(prehospital fluids and fluids given in the emergency department) as well as fluids given during the resuscitation in the ICU. Data from the BN system was stored and collected using the data files generated by the device for each patient. Primary crystalloid fluid calculations included only the predominant crystalloid (ex. Lactated Ringers) given in order to permit comparison to the Parkland formula. All/total fluids included any fluid given to the patient, including colloid adjuncts, enteral fluids, and intravenous drip medications given during the resuscitation. To compare fluid infusion volumes to the Parkland formula (4 ml/kg/TBSA) [9] and the Ivy Index (250ml/kg) [10], infusion volumes are presented in both ml/kg/TBSA and ml/kg. In order to account for patients who presented in a delayed fashion to the burn center, 24 continuous hours of resuscitation data were collected regardless of what hour post-burn the patient presented to the burn center. Analysis of fluid volumes was performed on data extracted from the BN system and not the EMR. These data provide a more accurate representation of actual hourly volumes infused during the resuscitation period as they were recorded during device use.

Patients were classified as either having "followed" the BN (FBN) recommendations or not (NFBN). A patient was considered as having "followed" the recommendations if the hourly infusion rates were within 20ml over or under of the BN system recommendations at least 83% of the time in the first 24 hours. Given that changes in fluid infusion rates for the patients are routinely performed on an hourly basis, there are only 24 possible recommendations that the system can generate during the initial resuscitation. There is no consensus on how much a clinical decision support tool, such as the Burn Navigator, should be utilized in order to be considered effective. In this study, because of the rapid development of an extracellular fluid deficit and resulting perturbations in patient physiology, we felt that providers should be given some leeway in following the recommendations 100% of the time (i.e. following all 24

recommendations during this phase). Therefore, we decided that patients in which the device was mostly used during this phase would be considered following the system. Patients in which the device was mostly not used, would be labeled as not having followed the device. For our case, we considered less than or equal to 4 deviations out of the initial 24 device recommendations would still fall under the following device (FBN) category, which would be 83% agreement. Complications data were collected on those associated with under- or over-resuscitation and diagnosed by a physician based on each burn center's clinical definition; no uniform definition was used across the sites. Documentation by a mid-level provider or physician in the electronic medical record of the complication was required. Common resuscitation-related complications were chosen for analysis in this study [11]. Under-resuscitation complications included burn shock, acute kidney injury, and myocardial infarction. Over-resuscitation complications included extremity compartment syndrome, abdominal compartment syndrome, intraocular compartment syndrome, acute respiratory distress syndrome, and atrial fibrillation. The time used for diagnosis was when it was documented in the medical record. In addition, overall and 28-day mortality were also collected.

Statistical methods: Analyses were carried out using ANOVA to test for differences in continuous measures between the groups, and the chi-square test was used for categorical measures. Posthoc Tukey adjusted pairwise comparisons were completed for measures that were significant overall. Given a larger sample size in this multicenter study, we chose to present data more representatively as means +/-SD, or medians [IQR] as appropriate [12,13].

Results

Participants: The study was able to meet its patient target goal of 300 patients. This included a combination of 111 retrospective and 189 prospective patients across the 5 participating centers

from November 2014 to June 2020. Two hundred eighty-five patients met inclusion criteria for analysis of resuscitation volumes during the first 24-hours after burn injury. Fifteen patients were excluded as they had no device data or had less than 10 hours of BN device data recorded (Figure 1).

Descriptive data: Table 1 shows the overall cohort demographic and relevant burn characteristics, broken out by patients who followed the BN system and those who did not. With the exception of age, there was no significant difference between the FBN and NFBN groups. There was a significant difference of in age between the FBN group and the NFBN group (48.3 ± 17.3 years vs. 42.6 ± 15.9 years, p=0.04). We believe that this 5-year difference between cohorts is only minimally clinically significant acknowledging the impact of age on mortality after burn injury and did not affect other analyses.

Main outcomes data: The volume of primary crystalloid fluid, all fluids given in the first 24 hours of resuscitation, as well as 24 hours of continuous resuscitation regardless of time of initiation after burn injury resulted in primary crystalloid volumes similar to the Parkland formula and overall fluid infusion volumes well under the Ivy index (Table 2). Delayed presentation resulted in higher primary crystalloid and overall fluid volumes compared to the immediate resuscitation group (Table 2). There was no significant difference in fluid volumes infused when comparing retrospective and prospective patients.

Inhalation injury occurred in 70 patients (24.6%). Patients with inhalation injury required 4.42 ± 1.83 ml/kg/TBSA of primary crystalloid fluid (204.62 ± 93.89 ml/kg in total fluids) compared to non-inhalation injury patients 3.96 ± 1.73 ml/kg/TBSA primary crystalloid (165.37 ± 89.80 ml/kg in total fluids) ($p = 0.05$, $p = 0.002$, respectively).

Analysis of FBN and NFBN were also performed. Patients in both groups had mean volumes similar to the Parkland formula at the 24-hour time point (Table 3). When the BN device recommendations were considered as followed, they were followed an average of 92.5 ± 8.5 percent of the time. Of those considered not followed, they had an average agreement rate of 50.4 ± 16.9 percent.

A similar comparison was performed for delayed presentations, which demonstrated results similar to delayed presentations in the first 24 hours, which was receiving greater primary and overall fluid volumes (Table 4).

Other analyses: Complications data are presented in Tables 5 and 6 as incidence of resuscitation-related complications. There were 39 patients who experienced more than one complication and 61 patients experienced one complication. There was a significantly decreased incidence of burn shock in the BN-guided versus the non-BN-guided group. Patients in whom burn shock was diagnosed received greater than the Parkland formula in primary crystalloid fluid and were approaching the Ivy index for total fluids, suggesting that they were not under-resuscitated (Table 6). Patients with abdominal compartment syndrome demonstrated evidence of over-resuscitation with a primary crystalloid volume of 322.06 ± 89.61 ml/kg and total fluids infused of 355.91 ± 104.26 ml/kg. Three patients underwent torso escharotomies and two patients ultimately required decompressive laparotomies. The remainder of over-resuscitation morbidities did not have fluid volumes infused over the Ivy index. There was a trend toward a decreased incidence of ARDS in the Followed Navigator group, fortunately the incidence was low in both groups after injury.

Overall mortality was 21.1% and 28-day mortality was 14%. While the difference in overall mortality between those who followed the BN and those who did not was significant, the

difference in mortality in the first 28 days was similar between the groups (Table 5). The median time to death was 21 days (IQR 7.8, 32) for overall mortality and 9.5 days (IQR 4.8, 21) in the 28-day mortality group.

Discussion

This study revealed that the Burn Navigator is a safe and effective tool for assisting in the fluid resuscitation of patients with large burn injuries when deployed to multiple burn centers. The system provides a software-based approach that allows providers to better manage the fluid intake of burn patients while providing the additional benefit of using advanced graphical user interface tools to better visualize the progression of the resuscitation of the patients during the acute phase after burn injury (Figure 2).

Primary fluid volumes in this study (4.07 ml/kg/TBSA) were similar to the Parkland formula and total fluid infusion volumes were slightly higher (4.68 ml/kg/TBSA) and remained under 5ml/kg/TBSA and under the Ivy index. This finding contrasts a large literature search performed over 35 years of burn resuscitation, in which 39 out of 48 studies (81%) found that 24-hour fluid volumes were in excess of the Parkland formula [14]. The fact that this study's participating centers have helped swing the pendulum back towards a final total volume comparable to the Parkland formula may be attributed to the BN's aggressive resuscitation strategy and to the evolution of burn care. In view of all the potential differences in practice existing among the five burn centers, we believe that the BN played an important role to help decrease provider variability during resuscitation and therefore avoid extraneous fluid volume. Burn resuscitation continues to improve with a focus on avoiding potentially lethal over-resuscitation complications and advances in critical care medicine, such as the improved ease of use of organ support

technologies, such as renal replacement therapy, have permitted the use of less volume in burn resuscitation [11].

In order to validate the use of the system in a clinical setting, we needed to first differentiate when the provider used the system and followed the recommendations of the algorithms versus other cases in which the system was present during the resuscitation, but the provider did not actively follow the output of the device; therefore we established the 83% cut-off for agreement in the first 24 hours of resuscitation. We examined the extremes of agreement as well, comparing those who followed the BN 100% of the time to those who followed it less than 50% and found no significant differences in infusion rates compared to the 83% cut-off for agreement (data not shown).

When the patient presented in a delayed fashion to a burn center, they received significantly more fluid in the next 24 hours compared when they presented closer after burn injury (Table 2), regardless of whether the BN was followed. The feeling of "having to make up for lost time" is consistent with earlier studies, who have shown that delayed resuscitation is implicated as requiring more fluid [15, 16].

This analysis also revealed that fluids given in addition to the primary crystalloid fluid, which includes albumin, fresh frozen plasma, enteral fluids and all intravenous medications, provide a significant source of additional fluids during the resuscitation phase. In our case, when considering the total volume of fluid given to the patients in addition to the resuscitative fluid, the total amount increased by approximately 16% (151 ml/kg vs. 175 ml/kg). This shows that fluids other than the primary crystalloid fluid contributes a significant amount of volume to the overall resuscitation efforts and should be taken to account for these fluids as part of the overall

management of the patient during resuscitation. The Burn Navigator helps with this process by graphically displaying the additional fluids given.

One interesting point to note is related to the differences in age between the two groups. Our analysis showed that patients whose resuscitation followed the Navigator were significantly older than the group who did not follow the Navigator. Interestingly, there was no other significant differences in their demographic and injury characteristics. We postulate that the age difference may partially explain the increased overall mortality in the group where the BN was followed (perhaps due to less resilience to in-hospital complications). Given that 28-day mortality was similar between the two groups, we do not believe that BN adherence in the first 24-48 hours was a factor. Indeed, overall mortality occurred at a median of 21 days after injury, and was likely not related to the initial resuscitation or adherence to BN recommendations.

Complications in this study were a judgement call of the care team as variability exists with regards to the definition of many complications so this study provided the opportunity of the care team to present complications as they defined them. There was a decreased incidence of burn shock in the BN-followed group despite both groups having primary crystalloid infusion rates comparable to the Parkland formula and no statistically significant differences in fluids when measured in ml/kg/TBSA or ml/kg (data not shown). These data demonstrate that burn shock is multifactorial and not purely related to fluid infusion rates [17].

There remain certain complications that are intricately linked to fluid volumes administered. This study demonstrated a low incidence of abdominal compartment syndrome (n = 5), but these patients received a large volume resuscitation, with the primary fluids at 24 hours well over the Ivy Index at 322.06 $\pm$ 89.61 [9]. This was the only complication in our study with a massive fluid infusion, suggesting that multiple factors contribute to these other complications, such as a

profound systemic inflammatory response and intense fluid shifts between fluid compartments [17, 18].

Limitations: There was the lack of a control group as it was designed as an observational trial. To conduct meaningful analysis on the effectiveness of the BN, analyses were performed looking at burn providers who utilized the device for a majority of the resuscitation versus those who did not follow the recommendations provided. Future study should examine when these deviations occurred and if the timing of following the BN impacted resuscitation-related outcomes. An additional limitation is the use of both retrospective and prospective patients to reach the goal enrollment. Again, study into these two cohorts could provide valuable information about the evolution of burn resuscitation over time. Many centers have reported initial resistance of implementation of the Burn Navigator into their practice, reporting an additional documentation burden during an already busy time in the early care of a severely burned patient. However, it quickly has become widely accepted in many centers as a standard; the prospective against retrospective comparison may reflect this. A more thorough examination of resuscitation-related complications and associated interventions is also warranted in future studies.

Conclusion

The dependable fluid volume recommendations and ease of using the Burn Navigator reflect the potential benefits of a computerized decision support tool during the acute resuscitation phase after burn injury. The device provided volume recommendations comparable to burn experts and would likely be an effective decision support tool if utilized by non-burn experts to aid in providing a safe burn resuscitation. Further examination of the resuscitation data will yield more detail into the ideal burn resuscitation fluid volumes that will minimize risk of complications.

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References

[1] Alvarado R, Chung KK, Cancio LC, et al. Burn resuscitation. Burns 2009; 35: 4-14.

[2] Dulhunty JM, Boots RJ, Rudd MJ, et al. Increased fluid resuscitation can lead to adverse outcomes in major-burn injured patients, but low mortality is achievable. Burns 2008; 34: 1090-7.

[3] Pruitt BA Jr, Mason AD JR, Moncrief JA. Hemodynamic changes in the early post-burn patient: the influence of fluid administration and of a vasodilator (hydralazine). J Trauma 1971:; 11(1): 36-46.

[4] Baxter CR, Shires T. Physiologic Response to crystalloid resuscitation of severe burns. Ann N Y Acad Sci 1968; 150(3): 874-94.

[5] Pham TN, Cancio LC, Gibran NS. American Burn Association Practice Guidelines: Burn Shock Resuscitation. J Burn Care Res 2008; 29(1): 257-66.

[6] Saffle JR. The Phenomenon of "Fluid Creep" in Acute Burn Resuscitation. J Burn Care Res 2007; 28: 382-95.

[7] Salinas J, Chung KK, Mann, EA, et al. Computerized decision support system improves fluid resuscitation following severe burns: An original study. Crit Care Med 2011; 39: 2031-8.

[8] Vandenbrouke JP, von Elm E, Altman DG, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. PloS Med 2007; 4(10): e297

[9] Baxter CR, Shires T. Physiological response to crystalloid resuscitation of severe burns. Ann N Y Acad Sci 1968;150(3): 874–94.

[10] Ivy ME, Atweh NA, Palmer J, et al. Intra-abdominal Hypertension and Abdominal Compartment Syndrome in Burn Patients. J Trauma 2000; 49(3): 387-91.

[11] Cancio LC. Initial assessment and fluid resuscitation of burn patients. Surg Clin North Am 2014; 94(4): 741-54.

[12] Glass GV, Peckham PD, Sanders JR. Consequences of Failure to Meet Assumptions Underlying the Fixed Effects Analyses of Variance and Covariance. Review of Educational Research. 1972;42(3):237-88.

[13] Lumley T, Diehr P, Emerson S, Chen L. The Importance of the Normality Assumption in Large Public Health Data Sets. Annu Rev Public Health 2002; 23: 151-9.

[14] Shah A, Pedraza I, Mitchell C, et al. Fluid volumes infused during burn resuscitation 1980-2015: A quantitative review. Burns 2020; 46: 52-7.

[15] Chung KK, Wolf SE, Cancio LC, et al. Resuscitation of Severely burned Military Casualties: Fluid Begets More Fluid. J Burn Care Res 2009; 67(2): 231-7.

[16] Pruitt BA Jr. Fluid and electrolyte replacement in the burned patient. Surg Clin North Am 1978: 58: 1291-312.

[17] Pham TN, Cancio LC, Gibran NS. American Burn Association Practice Guidelines: Burn Shock Resuscitation. J Burn Care Res 2008; 29(1): 257-66.

[18] Pruitt BA Jr. Protection from excessive resuscitation; “pushing the pendulum back.” J Trauma 2000; 49(3): 567-8.

Figure Legends

Figure 1. Patient enrollment flowchart for the study. Pro – prospective, Retro – retrospective, h – hours, BN – Burn Navigator

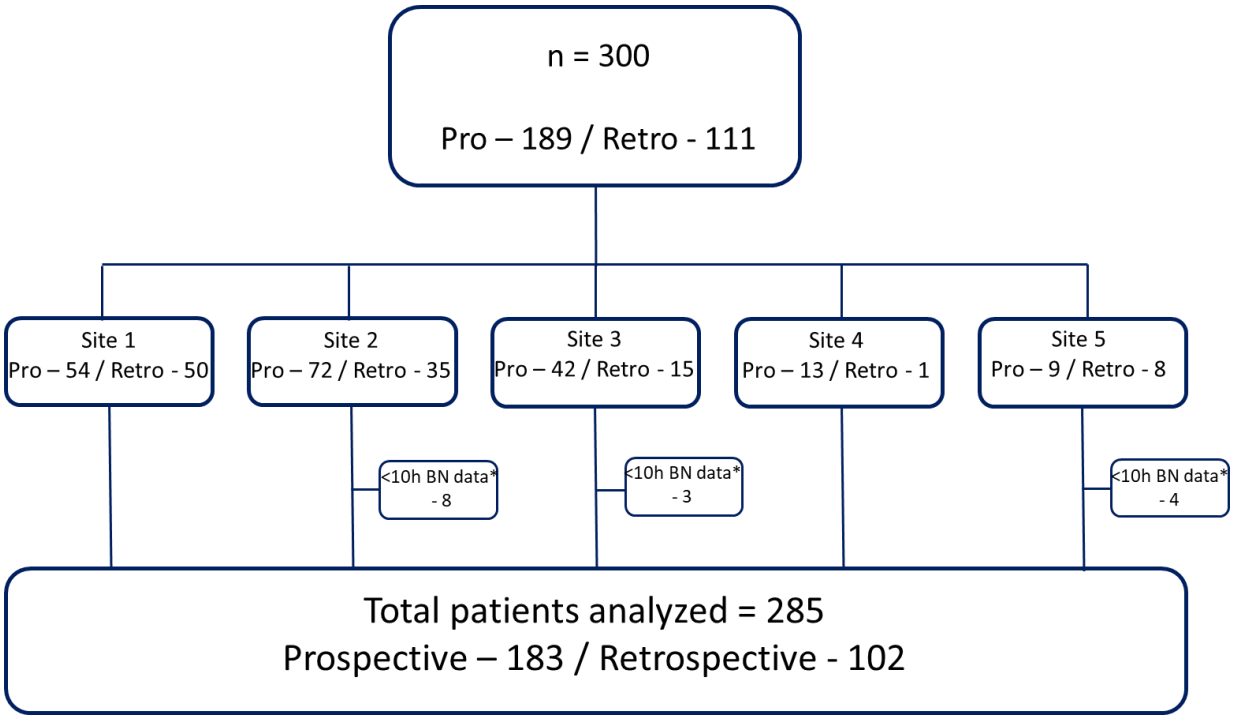

Figure 2. Sample display of the Burn Navigator depicting the hourly intake and output with legend and overall resuscitation, showing different resuscitation formulas and the Ivy index thresholds.

Demographic/Characteristic	All patients (n = 285)	Followed Navigator (n = 146)	Did Not Follow (n = 139)	p-value
Age	45.6 ± 16.8	48.3 ± 17.3	42.6 ± 15.9	0.04
TBSA	39.2 ± 17.7	39.1 ± 19	39.3 ± 16.2	0.90
% Full-thickness (median, IQR)	10 (1.9, 24.2)	9.5 (1.6, 24.9)	10 (1.9, 21.9)	0.93
BMI	29.0 ± 7.0	29.1 ± 7.2	28.9 ± 6.9	0.87
% Inhalation injury (n, %)	70 (24.6%)	29 (19.9%)	41 (29.5%)	0.16
ISS	21.2 ± 12.8	20.9 ± 13.2	21.6 ± 12.4	0.64

Table 1. Demographic and burn characteristics of patients in the study. Mean values ± standard deviation or median (IQR) presented as appropriate. TBSA = total body surface areas, BMI = body mass index, ISS = injury severity score. Data are presented as means +/- SD unless otherwise indicated.

Mean fluid volumes in the first 24 hours post-burn for all patients (n=285)		
	ml/kg/TBSA	**ml/kg**
Primary Crystalloid only	4.07 ± 1.76	151.48 ± 77.46
All fluids	4.68 ± 2.06	175.01 ± 92.22
Mean fluid volumes in first 24 hours after admission for subset with delayed presentation (n=230, median time to arrival= 6.5 hours)		
Primary Crystalloid only	5.28 ± 2.54	201.11 ± 106.53
All fluids	6.35 ± 2.95	244.08 ± 133.50

Table 2. Resuscitation fluid volumes for all patients (n=285) in the first 24 hours post-burn as well as mean fluid volumes in the first 24 hours after admission for the subset of patients who presented in a delayed fashion (n=230). Data are presented as mean ± SD.

	Followed Navigator (n = 146)	Did not Follow Navigator (n = 139)	p-value
Primary crystalloid fluid only ml/kg/TBSA	4.04 ± 1.62	4.11 ± 1.9	0.75
Primary crystalloid fluid only ml/kg	148.88 ± 76.50	154.21 ± 78.64	0.56
All fluids ml/kg/TBSA	4.63 ± 1.87	4.73 ± 2.26	0.68
All fluids ml/kg	172.10 ± 91.96	178.07 ± 92.73	0.59

Table 3. Comparison of resuscitation volumes between FBN and NFBN cohorts in the first 24 hours. Data are presented as means ± SD.

	Followed Navigator (n = 110)	Did not Follow Navigator (n = 120)	p-value
Primary crystalloid fluid only ml/kg/TBSA	5.45 + 2.94	5.12 + 2.12	0.33
Primary crystalloid fluid only ml/kg	213.71 + 122.43	189.56 + 88.47	0.08
All fluids ml/kg/TBSA	6.45 + 3.28	6.25 + 2.63	0.62
All fluids ml/kg	256.23 + 151.31	232.95 + 114.30	0.19

Table 4. Comparison of resuscitation volumes between FBN and NFBN cohorts over 24 after admission, regardless of when patients arrived at the burn center. Patients in this cohort presented at a median of 6.5 hours after injury. Data are presented as means $\pm$ SD.

Morbidity	Incidence (%)	Followed Navigator	Did not Follow	p-value
Under Resuscitation Morbidities				
Shock	47 (16.5%)	15	32	0.014
Acute kidney injury	34 (11.9%)	17	17	0.14
Myocardial infarction	3 (1.1%)	1	2	0.48
Over Resuscitation Morbidities				
Extremity compartment syndrome	39 (13.7%)	17	22	0.51
Abdominal compartment syndrome	5 (1.8%)	2	3	0.31
Intraocular compartment syndrome	13 (4.6%)	4	9	0.09
Acute respiratory distress syndrome	9 (3.2%)	7	2	0.07
Atrial fibrillation	2 (0.7%)	0	2	0.38
Mortality	60 (21.1%)	37	23	0.02
28-day Mortality	40 (14.0%)	22	18	0.49

Table 5. Incidence of resuscitation-related morbidities. Data are presented as n (%) of total morbidities.

	Shock (n = 47)	Acute kidney injury (n =34)	Extremity compartment syndrome (n = 39)	Abdominal compartment syndrome (n = 5)	Intraocular compartment syndrome (n = 13)	Acute respiratory distress syndrome (n = 9)
Age	46.3 ± 17.2	48.6 ± 19.0	41.6 ± 16.1	42.6 ± 22.4	39.4 ± 12.3	44.2 ± 15.8
BMI	29.1 ± 7.6	29.9 ± 6.1	28.6 ± 7.9	23.3 ± 2.9	29.1 ± 7.4	31.6 ± 8.1
TBSA (median, IQR)	44 (35,53 .5)	55 (30, 73.75	45 (35, 62.5)	53 (41, 64)	50 (40, 70)	65 (32, 80)
Percent Full-thickness (median, IQR)	12.1 (1.2, 39.5)	19.2 (0.9, 51.5)	25 (12.4, 49.3)	43.7 (29, 47.5)	43.1 (32, 47.5)	31.5 (22.5, 56)
Time after injury (hours)	10.8 (5.7, 22.1)	16.3 (9.2, 26.4)	10.0 (4.9, 17.4)	19.5 (17.1, 34.2)	11.1 (8.9, 15.8)	2.6 (1.0, 12)
%agree BN	60.9 ± 23.3	68.8 ± 28.4	66.9 ± 23.7	61.2 ± 27.9	56.1 ± 24.2	85.0 ± 21.3
Primary crystalloid fluid only ml/kg/TBSA	4.49 ± 1.78	3.94 ± 1.99	4.11 ± 1.59	6.50 ± 2.46	4.27 ± 1.55	4.25 ± 1.69
Primary crystalloid fluid only ml/kg	190.67 ± 61.69	189.65 ± 83.48	186.49 ± 68.24	322.06 ± 89.61	217.67 ± 87.63	220.56 ± 84.63
All fluids ml/kg/TBSA	5.27 ± 2.07	4.55 ± 2.19	4.80 ± 1.86	7.21 ± 2.84	4.87 ± 1.69	4.82 ± 2.11
All fluids ml/kg	223.87 ± 74.84	221.69 ± 95.81	219.26 ± 81.48	355.91 ± 104.26	248.41 ± 103.32	250.02 ± 99.59

Table 6. Demographics, burn and fluid resuscitation characteristics of patients who experienced resuscitation-related complications. Data are presented as means ± SD unless otherwise indicated.

The Battle of the Titans – Comparing Resuscitation Between 5 Major Burn Centers Using the Burn Navigator

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ABSTRACT

Introduction: The goal of burn resuscitation is to provide the least amount of fluid necessary to maintain end-organ perfusion and prevent burn shock. The objective of this analysis was to examine how the Burn Navigator (BN), a clinical decision support tool in burn resuscitation, was utilized across 5 major burn centers in the United States.

Methods: A non-interventional, observational trial of 300 adult patients with embedded prospective and retrospective components was undertaken to examine the effectiveness of the BN in burn resuscitation. 5 ABA-verified burn centers enrolled patients. Data examining patient demographics, burn characteristics, fluid volumes, and resuscitation-related complications were examined. Statistical analysis compared the 5 sites in terms of these variables.

Results: A total of 285 patients were eligible for analysis. There was no difference among the centers in terms of average age (45.5 $\pm$ 16.8 years), BMI (29.2 $\pm$ 6.9), ISS (21.2 $\pm$ 12.8), or median TBSA (34 [25.8, 47]). Primary crystalloid infusion volumes at 24 hours differed significantly when measured in ml/kg/TBSA (median 3.7 [2.9, 8.8], range 1.3 to 12.3). Similarly, total fluids, which includes colloid adjuncts, drip medications and enteral fluids, differed between groups when measured in both ml/kg (median 149.8 [106.5, 224.1], range 38.4 to 536.2) and ml/kg/TBSA (4.2 [3.3, 5.5], 1.7 to 15.3) at 24 hours. Post-hoc adjustment for pairwise comparisons resulted in a loss of significance between most of the sites. There was a total of 156 resuscitation-related complications reported across the 5 sites with an average incidence of 44.4 % incidence.

Conclusion: The Burn Navigator appeared to standardize fluid resuscitations across 5 major US burn centers. With primary fluid volumes near the Parkland formula, the device can be utilized effectively in burn centers, and further study should exam the utility of this device in facilities that do not commonly treat burn injuries, as well as the battlefield.