Examining the Practice Culture of Fluid Resuscitation in Septic Neutropenic Adults

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June 3rd, 2020

Abstract

Sepsis is the result of a severe infection that causes over 270,000 hospital deaths annually in the United States (Centers for Disease Control, 2016). Neutropenic patients are significantly more susceptible to infection and mortality due to their lack of immune protection from pathogens (Kochanek et al., 2019). There are no neutropenic-specific management guidelines provided by the Surviving Sepsis campaign.

The hypotension support guidelines in the Surviving Sepsis Campaign provides specific instructions to rapidly infuse 30mL/kg of crystalloids and initiate norepinephrine (vasopressor) if the mean arterial pressure (MAP) drops below 65. These parameters are not always followed for various reasons such as provider preference, intensive care availability and central venous access. This survey will investigate providers' sepsis management tendencies based on hypothetical patient features, neutropenia and clinical data.

Keywords: Sepsis, neutropenic, fluid resuscitation

Introduction

Problem Description

Sepsis causes approximately 250,00 hospital deaths per year (Centers for Disease Control, 2016). Neutropenic [absolute neutrophil count (ANC) <2500] patients are at a higher risk of developing sepsis due to their immunocompromised state (Kochanek et al., 2019). Mortality rates approach 50% if neutropenic sepsis is left untreated for 48 hours or more (White & Ybarra, 2017). Blood pressure support with 30mL/kg of crystalloid fluid and parameter driven vasopressor administration are important aspects of the Surviving Sepsis campaign. These guidelines are not always strictly adhered to for various reasons including provider preference, lack of intensive care availability, lack of central venous access, and concern for fluid overload. Therefore, deviation from the Surviving Sepsis guidelines may be especially detrimental in septic neutropenic patients.

Available Knowledge

The Surviving Sepsis guidelines were first introduced in 2002. They have since been updated in 2008, 2012, and 2016 (Levy, Evans, & Rhoads, 2018). The 2016 version updates hypotensive support to consist of rapidly infusing 30mL/kg of crystalloids over two hours and initiation norepinephrine vasopressor if the MAP drops below 65.

The current definition of sepsis is based on the Sequential Organ Failure Assessment (SOFA) consensus statement stating sepsis is life-threatening organ dysfunction caused by dysregulated host-response to infection (Gul, Arslantas, Cinel, & Kumar, 2017). The updated definition and inclusion criteria were designed to detect patients who may present atypically with a septic infection by assessing for organ dysfunction. SOFA is scored from 0 to 24 and includes partial O2 (PaO2)/fraction of inspired O2 (FiO2) measurement, Glasgow coma scale (GCS) assessment, mean arterial pressure on or off pressor medication, bilirubin level, platelet count,

and creatine measurement. These values indicate the presence or absence of brain, lung, liver, kidney and cardiovascular function and or organ damage. A score of 11 or greater is associated with greater than 90% chance of death from sepsis. The quick SOFA (qSOFA) score is used to easily identify patients who may be septic but not yet admitted to the intensive care unit (ICU). Systolic blood pressure of less than or equal to 100, respiratory rate of greater than or equal to 22, and GCS of less than or equal to 14 all count for one point. Two or more points suggest that patient is septic and is associated with an increased length of stay in the hospital. (Gul, Arslantas, Cinel & Kumar, 2017).

Systemic inflammatory response syndrome (SIRS) scores were previously heavily utilized to screen for sepsis, but was proven to be less sensitive than the SOFA score (Seymour et al. 2016). SIRS criteria variables were included in this study to evaluate for significance in provider vasopressor management practices.

Sepsis is also defined on a severity continuum (Baccaglini et al., 2020). Severe sepsis is defined as sepsis plus organ dysfunction such as an acute kidney injury or shock liver. Septic shock is the most life-threatening form of sepsis in which mean arterial pressure is not maintained by crystalloid fluid support and the patient requires vasopressors to maintain MAP and organ perfusion.

A thorough search of relevant sepsis research highlights the lack of neutropenic-specific data. Neutropenia is defined as an absolute neutrophil count of less than 1.5×10^9/L (Lehman & Segal, 2020). Patients with low neutrophils lack the ability to mount an immune response to an invading pathogen, and therefore are highly susceptible to sepsis and septic shock.

Kochanek et al. (2019) addressed 26 aspects of sepsis and critical care comparing neutropenic patients to non-neutropenic patients and found no statistically significant changes in

treatment via literature review. Specifically, broad-spectrum antibiotics with pseudomonas coverage were recommended such as meropenem, imipenem-cilastatin and/or piperacillin-tazobactam. The authors found patients with septic shock had better outcomes when an anti-pseudomonal antibiotic such as meropenem was paired with an aminoglycoside such as vancomycin. There were no recommendations on using fluid boluses versus early vasopressors to maintain MAP. The authors also note a lack of neutropenic-specific randomly controlled trials (RTCs) to better evaluate for evidence. More research is needed on the effects of treatment in patients with disease and treatment related neutropenia.

Patel & Gruber (2015) performed a literature review of current treatment trends of sepsis and septic shock in patients with neutropenia and hematologic malignancies. Their recommendations about antimicrobial coverage and pseudomonas coverage are very similar to Kochanek et al. (2018). The importance of early fungemia detection and treatment was also highlighted. The authors recommend liposomal amphotericin B for invasive fungal infections and voriconazole for invasive pulmonary aspergillus.

Acute respiratory distress syndrome (ARDS) and mechanical ventilation requirements are serious sequelae of sepsis. Significant efforts are made to prevent intubation and mechanical ventilation in patients with sepsis. Patel and Gruber, 2015 found that non-invasive ventilation such as bilevel positive airway pressure (Bi-PAP) led to delayed intubation and increased association with ARDS. Hi-flow nasal cannula was associated with decreased rates of ARDS and is suggested in the septic neutropenic population instead of Bi-PAP (Patel & Gruber, 2015).

Rationale

Neutropenic patients are more susceptible to developing sepsis and dying if not treated properly (Kochanek et al., 2019). Blood pressure support is paramount in preserving organ

function. The Surviving Sepsis guidelines specify blood pressure support parameters, but providers do not always follow these instructions for various reasons including disease history, ICU availability, presence or absence of central line and confounding vital signs and laboratory data. Little research has been done to evaluate the effectiveness of these specific guidelines in neutropenic adults.

Specific Aims

The specific aims of this study were to evaluate if acute care providers change their blood pressure management based on a patient's neutropenic status. Additionally, providers were asked to comment on perceived barriers to vasopressor initiation.

Methods

Context

This was an anonymous emailed provider practice survey. Neutropenia was defined as an ANC of <2500. Surviving Sepsis guidelines were provided in the body of the survey for reference purposes.

Interventions

An online survey was emailed to OHSU oncology, internal medicine, emergency medicine, critical care, cardiology, and pulmonology physicians, nurse practitioners, and physician assistants. Seven questions were posed to the participants. The first question addressed the individual provider's amount of experience measured in years treating septic patients. The second question asked the provider to identify which area of medicine they spend at least 50% of their time (outpatient, acute care/wards, emergency medicine, critical care, or operating room). The third and fourth questions described a hypothetical patient scenario listing relevant clinical data including mean arterial pressure (MAP) of less than 60, 60 and trending down, 60 and

trending up, MAP of 65 or greater, lactate less than 4, lactate of 4, lactate greater than 4, heart rate 90 or greater, temperature 38.3 Celsius or higher, temperature of 36.0 or lower, presence or absence of central venous catheter, ANC (2500 or less), known recent sepsis or bacteremia, leukocytosis of 12,000 or more, altered mental status, tachypnea or respiratory rate greater than 21 breaths per minute.

The participants were asked to rank each clinical data point on a scale from very unlikely, unlikely, neutral, likely, to very likely in their role at influencing the provider to initiate vasopressors. The third question posed a hypothetical question regarding initial management of sepsis in an adult, prior to completion of initial fluid resuscitation. The fourth question asks the provider to rank the same clinical data points after initial fluid resuscitation with 30mL/kg of crystalloid. The fifth question asked the provider to select any of the following as perceived barriers of initiating vasopressor therapy: Difficulty identifying and managing sepsis, lack of ICU availability, prefer to continue crystalloid support beyond 30mL/kg, unfamiliar/uncomfortable managing vasopressors, institution-specific policy regarding sepsis management, lack of central venous access.

The sixth question asked the provider if a patient's neutropenic status changed their management of sepsis. A text box was provided for free-text answers. The seventh and final question provided a free text box for discussion of thoughts and comments about following Surviving Sepsis guidelines in the individual participant's practice. Providers were thanked for their participation and encouraged to email the investigator with questions or feedback.

Study of the Interventions

Measures

The survey measured providers' practice habits by asking them to rank clinical data points on a 5-point Likert-like scale of very unlikely, unlikely, neutral, likely or very likely. Likert-like scales are useful when investigating personal attitudes and beliefs (Duncombe, 2018). All questions were weighted equally, and responses were anonymous.

Each survey response was evaluated for completeness. 31 responses were received, 30 were complete. One response was excluded for lack of response to five of the seven questions. Data accuracy was ensured by excluding incomplete survey responses.

Analysis

The online platform Survey Monkey was used to collect data. Responses were recorded and analyzed using Excel spreadsheets and SPSS statistical analysis software. Variations in data were interpreted by their associations with provider length of experience and primary clinical setting. Linear regression ANOVA testing was performed on the most commonly chosen data points and measured against provider experience level to assess for association.

Ethical Considerations

This survey recorded anonymous provider responses via the electronic survey monkey platform. Provider experience and workplace setting were the only descriptive data collected. Personal identifying information was not collected. This survey posed no risks to its participants.

Results

This survey was designed and approved by the OHSU IRB on December 11, 2019 (Study #00020540). The survey was distributed to 130 providers on March 24, 2020 and closed to responses on April 25, 2020. 31 responses were collected. Half of the total responses were received by March 25, 2020.

Seventeen clinical variables were presented on a scale of very unlikely, unlikely, neutral, likely, and very likely to the respondents with the context of the question, “What would drive you to initiate vasopressors or not initiate vasopressors”. The Surviving Sepsis guidelines recommend vasopressor initiation based on MAP values (Levy, Evans, & Rhodes, 2018). The first variable was a MAP of less than 60. The mean response was likely, and the median response was also likely. The second variable was MAP of 60 and trending down. The mean response was likely, and the median response was very likely. The third variable presented was MAP of 60 and trending up. The mean response was unlikely, and the median response was also unlikely. The fourth variable presented was MAP of 65 or greater. The mean response was unlikely, and the median response was very unlikely.

Serum lactate levels are monitored to gauge effectiveness of fluid resuscitation and prognostication for septic shock severity (Levy, Evans, & Rhodes, 2018). The fifth variable presented was lactate level less than 4. The mean response was unlikely, and the median response was also unlikely. The sixth variable presented was a lactate level of 4. The mean response was neutral, and the median response was also neutral. The seventh variable presented was lactate greater than 4. The mean response was 3.5 meaning the respondents answered neutral and likely evenly. The median response was likely.

The remaining variables presented were elements of SIRS criteria, qSOFA score, neutropenia, and practical limitations such as presence or absence of a central line. The eighth variable presented was heart rate greater than 90. The mean response was unlikely, and the median response was also unlikely. The ninth variable presented was temperature greater than 38.3 Celsius. The mean response was neutral, and the median response was neutral. The tenth variable presented was temperature less than 36.0 Celsius. The mean response was neutral, and

the median response was also neutral. The eleventh variable was a respiratory rate of 22 or greater. The mean response was neutral, and the median response was also neutral. The twelfth variable presented was altered mental status from baseline. The mean response was neutral, and the median response was also neutral. The thirteenth variable presented was leukocytosis or total white blood cell count greater than 12,000. The mean response was neutral, and the median response was also neutral. The fourteenth variable presented was ANC less than 2500. The mean response was neutral, and the median response was also neutral. The fifteenth variable presented was the presence of a central line. The mean response was neutral, and the median response was also neutral. The sixteenth variable presented was the absence of a central line. The mean response was unlikely, and the median response was neutral. The seventeenth variable presented was known recent sepsis or bacteremia. The mean response was neutral, and the median response was likely (see Table C2).

The fourth question of the survey asked the respondents to rate fourteen variables on a patient after they had received the Surviving Sepsis mandated 30mL/kg volume of fluid resuscitation. Known recent bacteremia or sepsis was omitted and MAP values were condensed (see Table D2). Notable changes to provider variable responses were to MAP of less than 60. The mean and median changed to very likely. MAP under 65 and trending down also elicited a change in response to likely leading initiation of vasopressors. Additionally, a lactate greater than four after fluid resuscitation changed from neutral to likely initiation of vasopressors.

ANOVA analysis showed a non-statistically significant association between providers with less experience (0-5 years) and identifying hyperlactatemia (lactate >4) and known recent infection as likely triggers to initiate vasopressors. There was no association with provider length

of experience and choosing severe hypotension (MAP<60) likely representing the clinical significance of severe hypotension in vasopressor initiation.

The provider response timing and rate were likely limited due to national emergency response to Covid-19. The Covid-19 pandemic affected the United States and Oregon state medical system by prioritizing pandemic response, increasing provider exposure risk, and changing workflows to address increased patient volumes. All elective surgeries were cancelled at OHSU, leaving OR providers without their usual workflow. To address this challenge, three reminder survey invitations were sent with updated messaging highlighting the minimal time commitment required to complete the survey and the importance of continuing nursing research during a pandemic.

The majority of providers identified a select few of the variables presented as significant in their decision-making in sepsis resuscitation. A MAP less than 60 and lactate greater than 4 were the two factors most likely to lead a provider to initiate vasopressors. Known recent bacteremia or sepsis was also rated likely to lead a provider to initiate vasopressors. A MAP greater than 65 and lactate less than 4 were least likely to lead a provider to initiate vasopressors. Interestingly, a lactate of 4 and a patient's neutropenic status did not affect a provider's likelihood to initiate vasopressors.

Steps were taken to improve the survey completion rate, in response to the concurrent emergence of the Covid-19 global pandemic. Respondents were very unlikely to respond to the survey after the first day it was received. The survey was scheduled to be sent at 7am on a business day. The goal of an early email was to catch the provider's attention early in the workday before they became busy with patient care and other responsibilities. Sending the

survey later in the day or on a weekend resulted in much fewer responses. One respondent elected not to answer the clinical questions and responded to the free-text questions.

Discussion

Summary

This survey identified very few clinical variables strongly lead a provider to initiate or not initiate vasopressors. Severe hypotension (MAP less than 60), severe lactatemia (greater than 4), and known recent sepsis or bacteremia were the most clinically significant variables. Surprisingly, neutropenia and presence/absence of a central line were considered neutral variables when considering initiation of vasopressors. Interestingly, the Surviving Sepsis guidelines recommend initiating vasopressors at a MAP of 65 or less. The respondents in this survey found a MAP of 60 or less to be a clinical trigger for initiating vasopressors, likely representing adjusted clinical practice to lack of updated guidelines.

Association but not statistically significant correlation was seen between providers of less experience using hyperlactatemia and known recent infection as clinical indicators of vasopressor initiation. One might argue that increased provider experience leads to action based on less clinical data points and utilizes severe hypotension as a strong clinical indicator for initiating vasopressors.

Regarding neutropenia, ten providers reported in free text that neutropenia alone increases their likelihood of initiating vasopressors. Eleven providers reported neutropenic status does not affect their decision to initiate vasopressors. Providers reported considering additional risk when placing a central line on a neutropenic patient, transferring a patient to the ICU after the first failed fluid bolus, consulting infectious disease on any new case of neutropenic sepsis, using cefepime instead of piperacillin/tazobactam, and adding antifungal therapy when

addressing neutropenic sepsis. One provider commented that the 1-hour bundle was unobtainable, and the 3-hour bundle is “hard enough” citing systemic difficulty in timely sepsis identification and nursing support.

General provider comments about modifying Surviving Sepsis consisted of requesting a concise pocket-resource for quick access. Three providers reported the need for population-specific guidelines such as heart failure and neutropenia. One provider suggested tailoring the volume of fluid resuscitation to each patient instead of a generalized 30mL/kg bolus.

Strengths of this survey included its efficient design and mirroring of fast-paced decision making. This survey was designed to gather as much data as possible in five minutes. Acute and critical care providers are busy and do not have an excess of time for other work outside of patient care. Additionally, sepsis management is commonly a high-stress situation that leaves little time for consideration of initial management decisions.

Interpretation

Kochanek et al. (2019) revised the 2013 guidelines from the Infectious Disease Working Party and the Intensive Care Working Party of the German Society of Hematology and Oncology on sepsis management by performing a literature review on the available studies on neutropenic sepsis management (a total of six studies). The authors found there to be no evidence to support changing initial fluid resuscitation guidelines in the neutropenic population. This study also mentions the paucity of neutropenic-specific sepsis data and that more research is needed to create evidence-based neutropenic sepsis guidelines.

Patel and Gruber (2015) cite neutropenia alone to no longer be a risk factor in predicting poor outcome in intensive care admissions. They do, however, cite neutropenic sepsis to commonly be the result of polymicrobial infections that are resistant to antibiotics, leading to

increased morbidity and mortality. This change in perceived risk highlights the need for antimicrobial stewardship and avoidance of hospital acquired infections, in addition to early detection of sepsis.

Finally, Reilly et al. (2016) performed a prospective cohort study on neutropenic sepsis patients admitted to the ICU. They found neutropenia to be an independent risk factor for acute kidney injury, but not acute respiratory distress syndrome or 30-day mortality.

Neutropenia was found to be a neutral factor when providers were considering initiating vasopressors in the survey. Objective hypotension and hyperlactatemia were the most significant variables providers identified for vasopressor initiation decision-making. Subjective free-text comments highlighted the need for neutropenic and disease-specific sepsis management guidelines.

This project's specific aims were to identify provider practice cultures in sepsis management, if neutropenia affected their decision making, and if factors reported by providers were in line with the Surviving Sepsis guidelines. Neutropenia was reported as a neutral factor when considering initiation of vasopressors. This was an unexpected outcome and may support the current guidelines blanket guidelines instead of population-specific guidelines. The provider responses of factoring severe hypotension (MAP less than 60) and severe hyperlactatemia (lactate greater than 4) were the two factors most likely to lead a provider to initiate vasopressors. These factors increased in likelihood after hypothetical fluid resuscitation.

The expected outcomes differed slightly from the actual outcomes. Mainly, only two clinical data points proved to be significant to the responding providers of this survey. Severe hypotension (MAP less than 60 or less than 65 and trending down) and hyperlactatemia (lactate greater than 4) lead providers to initiate vasopressors in my clinical scenarios. Interestingly, a

lactate of 4 which is defined by the Surviving Sepsis guidelines to be an indicator of septic shock and indication of vasopressors was a neutral factor in determining the need for vasopressors in this study. Neutropenia was not identified as an independent factor for initiating vasopressors which was an unexpected outcome. The provider comments, however, highlighted a need for population-specific sepsis guidelines including neutropenia. Seventeen out of twenty-nine responses indicate they change their management of sepsis based on neutropenic status. Four of those twenty-nine specifically initiate ICU care and vasopressors sooner than a non-neutropenic patient.

This project could be improved upon and extended by narrowing the clinical case presentation to focus solely on provider opinions on hypotension. Further retrospective research examining lower thresholds of MAP for vasopressor initiation could be implemented to inform and update the Surviving Sepsis guidelines.

Limitations

The major limitation of this study was response rate. The response rate goal was 30% of the total respondents include which is an n of 60. This study had a lower than desirable response rate with an n of 31. Unfortunately, extenuating circumstances such as the initial response to the Covid-19 pandemic and dynamic change to the Oregon health system likely diminished providers' availability to complete the survey.

This survey was designed to imitate a clinical scenario where sepsis had been detected and asked providers to rank individual clinical data points on a Likert-like scale. This survey was challenging to design because the aim was to identify if neutropenia changes provider management. A narrower focused clinical question would like gather more data on specific hypotension management. One free-text comment was received about difficulty conceptualizing

the clinical scenario presented. The survey design was generalized in an attempt to decrease provider response bias which in resulted in generalized results with clarification in the comments.

Minimizing bias was integral in the design of this survey. Therefore, a generalized clinical scenario was presented without specific patient history to attempt to record true provider management decisions based on the concrete data presented. Therefore, this study design was successful preventing a biased neutropenia-led vasopressor initiation response and likely gathered accurate data about how providers manage sepsis when focusing on concrete clinical data.

Conclusions

The results of this survey highlight the difficulty providers face when managing sepsis. Neutropenic status was reported to be an important factor to consider when making management choices per the comments, but considered a neutral factor when providers were asked to make data-driven management decisions. This shows the need for continued research for more evidence-based neutropenic sepsis guidelines.

The necessity for disease-specific sepsis management research is supported by many citations in this paper and provider survey comments. For example, heart failure causes approximately 80,000 deaths per year in the United States and does not have sepsis-specific management guidelines (Jackson et al., 2018). Kochanek et al. (2019), Jackson et al. (2018), Reilly et al. (2016), and provider respondents from this survey necessitate the importance of research of disease-specific sepsis management to improve outcomes.

The results of this survey support the continued use of the Surviving Sepsis Guidelines in the management of neutropenic sepsis. Providers survey responses support the use of the clinical

measures of severe hypotension and hyperlactatemia as described in the guidelines as data-driven indications to initiate vasopressors. Provider comments support research into disease-specific sepsis management guidelines.

Further study is necessary in describing if disease-specific management guidelines would change sepsis outcomes. For example, a subsequent provider survey could pose a clinical question about a septic patient with no known medical history, one with heart failure, and one with neutropenia. Those results could be analyzed to determine providers' management decisions based on disease context in addition to vital signs and lab values. Also, a retrospective study could be performed to investigate if a lower MAP threshold (<65) changed sepsis mortality to update the Surviving Sepsis guidelines.

Funding

No funding was required to implement this study. The writer of the proposal was the sole investigator and performed the data collection and statistical analyses without outside funding.

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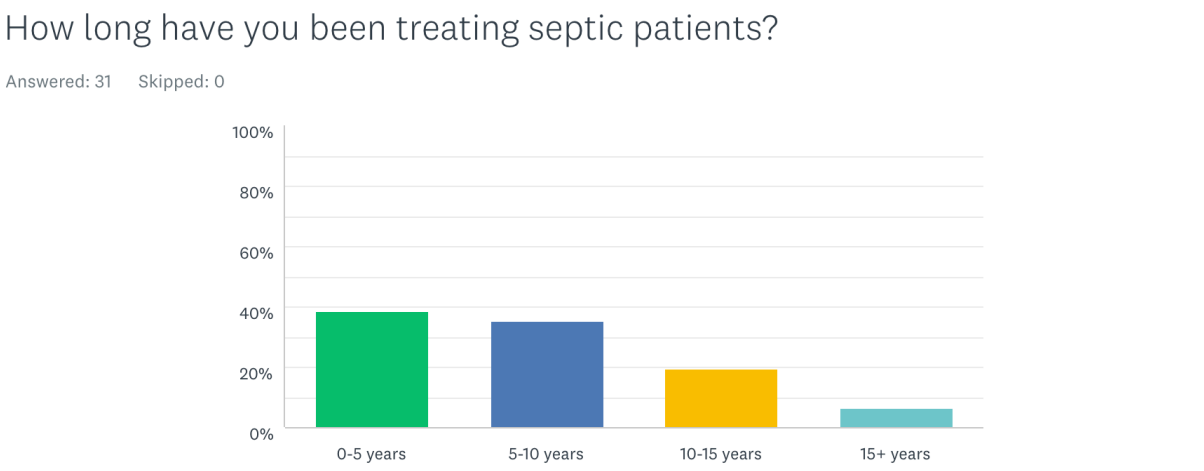
Appendix A

Bar graph depicting provider length of experience



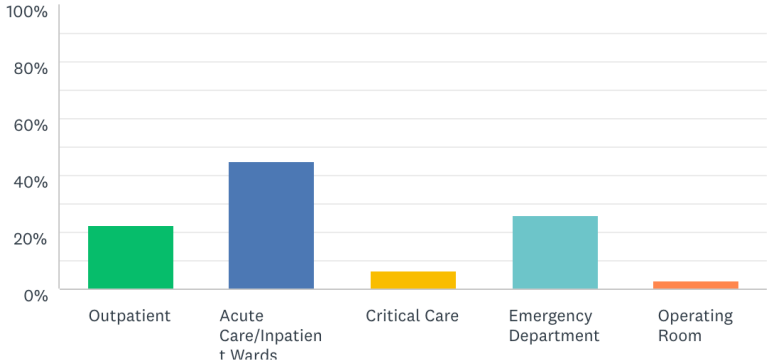
ANSWER CHOICES	RESPONSES	
0-5 years	38.71%	12
5-10 years	35.48%	11
10-15 years	19.35%	6
15+ years	6.45%	2
Total Respondents: 31		

Appendix B

Bar graph depicting provider area of clinical care

Choose one answer: Which area do you spend >50% of your time treating patients?

Answered: 31 Skipped: 0



ANSWER CHOICES	RESPONSES	
Outpatient (1)	22.58%	7
Acute Care/Inpatient Wards (2)	45.16%	14
Critical Care (3)	6.45%	2
Emergency Department (4)	25.81%	8
Operating Room (5)	3.23%	1
Total Respondents: 31		

BASIC STATISTICS

Minimum	Maximum	Median	Mean	Standard Deviation
1.00	5.00	2.00	2.44	1.17

Appendix C

Bar graph depicting provider responses to initial clinical sepsis management question

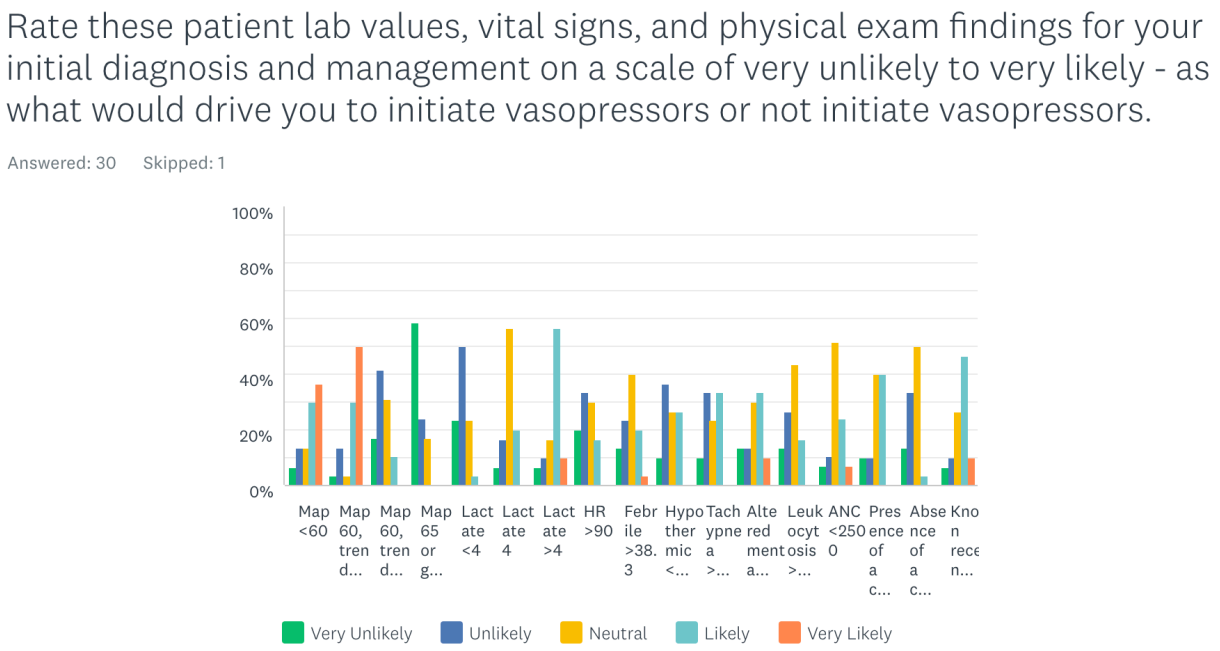


Figure C1

Respondent responses to clinical question one

	VERY UNLIKELY (1)	UNLIKELY (2)	NEUTRAL (3)	LIKELY (4)	VERY LIKELY (5)	TOTAL	WEIGHTED AVERAGE
Map <60	6.67% 2	13.33% 4	13.33% 4	30.00% 9	36.67% 11	30	3.77
Map 60, trending down	3.33% 1	13.33% 4	3.33% 1	30.00% 9	50.00% 15	30	4.10
Map 60, trending up	17.24% 5	41.38% 12	31.03% 9	10.34% 3	0.00% 0	29	2.34
Map 65 or greater	58.62% 17	24.14% 7	17.24% 5	0.00% 0	0.00% 0	29	1.59
Lactate <4	23.33% 7	50.00% 15	23.33% 7	3.33% 1	0.00% 0	30	2.07
Lactate 4	6.67% 2	16.67% 5	56.67% 17	20.00% 6	0.00% 0	30	2.90
Lactate >4	6.67% 2	10.00% 3	16.67% 5	56.67% 17	10.00% 3	30	3.53
HR >90	20.00% 6	33.33% 10	30.00% 9	16.67% 5	0.00% 0	30	2.43
Febrile >38.3	13.33% 4	23.33% 7	40.00% 12	20.00% 6	3.33% 1	30	2.77
Hypothermic <36.0	10.00% 3	36.67% 11	26.67% 8	26.67% 8	0.00% 0	30	2.70
Tachypnea >20 RR/minute	10.00% 3	33.33% 10	23.33% 7	33.33% 10	0.00% 0	30	2.80
Altered mental status (from baseline)	13.33% 4	13.33% 4	30.00% 9	33.33% 10	10.00% 3	30	3.13
Leukocytosis >12,000 WBC	13.33% 4	26.67% 8	43.33% 13	16.67% 5	0.00% 0	30	2.63
ANC <2500	6.90% 2	10.34% 3	51.72% 15	24.14% 7	6.90% 2	29	3.14
Presence of a central line	10.00% 3	10.00% 3	40.00% 12	40.00% 12	0.00% 0	30	3.10
Absence of a central line	13.33% 4	33.33% 10	50.00% 15	3.33% 1	0.00% 0	30	2.43

Table C2

Basic statistics of clinical question one responses

BASIC STATISTICS

	MINIMUM	MAXIMUM	MEDIAN	MEAN	STANDARD DEVIATION
Map <60	1.00	5.00	4.00	3.77	1.26
Map 60, trending down	1.00	5.00	4.50	4.10	1.16
Map 60, trending up	1.00	4.00	2.00	2.34	0.88
Map 65 or greater	1.00	3.00	1.00	1.59	0.77
Lactate <4	1.00	4.00	2.00	2.07	0.77
Lactate 4	1.00	4.00	3.00	2.90	0.79
Lactate >4	1.00	5.00	4.00	3.53	1.02
HR >90	1.00	4.00	2.00	2.43	0.99
Febrile >38.3	1.00	5.00	3.00	2.77	1.02
Hypothermic <36.0	1.00	4.00	3.00	2.70	0.97
Tachypnea >20 RR/minute	1.00	4.00	3.00	2.80	1.01
Altered mental status (from baseline)	1.00	5.00	3.00	3.13	1.18
Leukocytosis >12,000 WBC	1.00	4.00	3.00	2.63	0.91
ANC <2500	1.00	5.00	3.00	3.14	0.94
Presence of a central line	1.00	4.00	3.00	3.10	0.94
Absence of a central line	1.00	4.00	3.00	2.43	0.76
Known recent sepsis or bacteremia	1.00	5.00	4.00	3.43	1.02

Table C3

Appendix D

Bar graph depicting provider responses to initial 17-variable clinical question

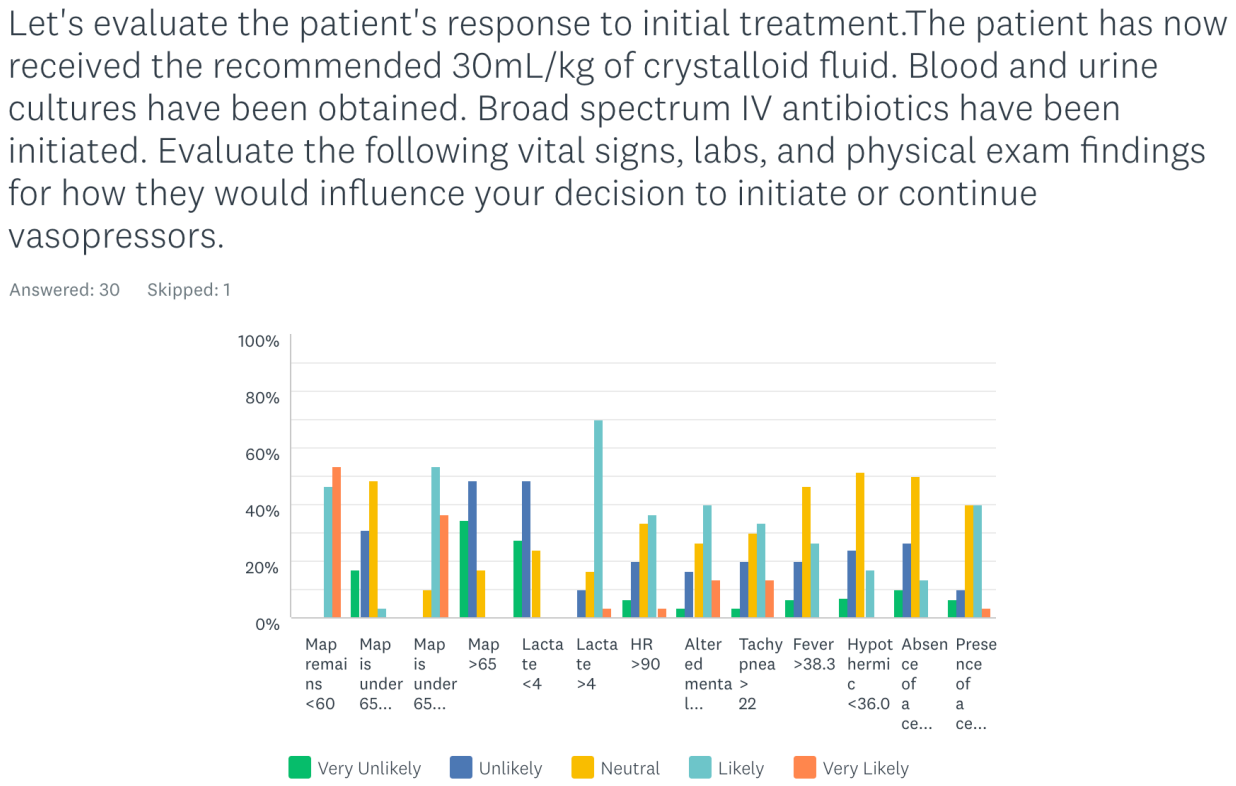


Figure D1

Responses of clinical question two

	VERY UNLIKELY (1)	UNLIKELY (2)	NEUTRAL (3)	LIKELY (4)	VERY LIKELY (5)	TOTAL
Map remains <60	0.00% 0	0.00% 0	0.00% 0	46.67% 14	53.33% 16	30
Map is under 65 and trending up	17.24% 5	31.03% 9	48.28% 14	3.45% 1	0.00% 0	29
Map is under 65 and trending down	0.00% 0	0.00% 0	10.00% 3	53.33% 16	36.67% 11	30
Map >65	34.48% 10	48.28% 14	17.24% 5	0.00% 0	0.00% 0	29
Lactate <4	27.59% 8	48.28% 14	24.14% 7	0.00% 0	0.00% 0	29
Lactate >4	0.00% 0	10.00% 3	16.67% 5	70.00% 21	3.33% 1	30
HR >90	6.67% 2	20.00% 6	33.33% 10	36.67% 11	3.33% 1	30
Altered mental status	3.33% 1	16.67% 5	26.67% 8	40.00% 12	13.33% 4	30
Tachypnea > 22	3.33% 1	20.00% 6	30.00% 9	33.33% 10	13.33% 4	30
Fever >38.3	6.67% 2	20.00% 6	46.67% 14	26.67% 8	0.00% 0	30
Hypothermic <36.0	6.90% 2	24.14% 7	51.72% 15	17.24% 5	0.00% 0	29
Absence of a central line	10.00% 3	26.67% 8	50.00% 15	13.33% 4	0.00% 0	30
Presence of a central line	6.67% 2	10.00% 3	40.00% 12	40.00% 12	3.33% 1	30

Table D2

Basic statistics of clinical question two responses

BASIC STATISTICS

	MINIMUM	MAXIMUM	MEDIAN	MEAN	STANDARD DEVIATION
Map remains <60	4.00	5.00	5.00	4.53	0.50
Map is under 65 and trending up	1.00	4.00	3.00	2.38	0.81
Map is under 65 and trending down	3.00	5.00	4.00	4.27	0.63
Map >65	1.00	3.00	2.00	1.83	0.70
Lactate <4	1.00	3.00	2.00	1.97	0.72
Lactate >4	2.00	5.00	4.00	3.67	0.70
HR >90	1.00	5.00	3.00	3.10	0.98
Altered mental status	1.00	5.00	4.00	3.43	1.02
Tachypnea > 22	1.00	5.00	3.00	3.33	1.04
Fever >38.3	1.00	4.00	3.00	2.93	0.85
Hypothermic <36.0	1.00	4.00	3.00	2.79	0.80
Absence of a central line	1.00	4.00	3.00	2.67	0.83
Presence of a central line	1.00	5.00	3.00	3.23	0.92

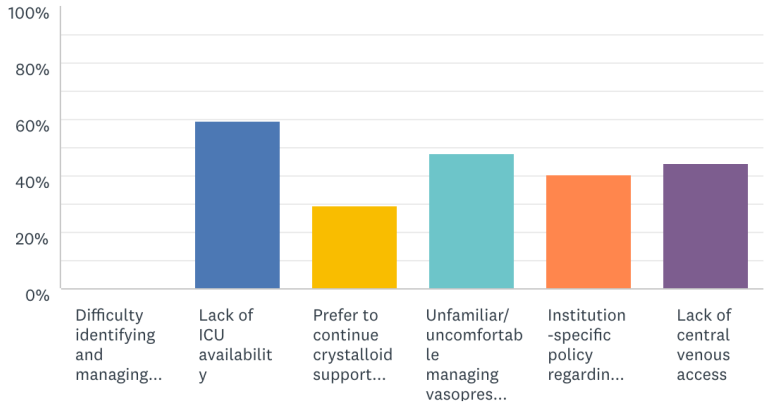
Table D3

Appendix E

Bar graph depicting provider barriers to initiating vasopressor therapy

What are the barriers to initiating vasopressor therapy?Here is a link to a quick and easy Surviving Sepsis resource. https://www.grepmed.com/images/4539/survivingsepsis-resuscitation-criticalcare-management-onehour-bundle-1hour

Answered: 27 Skipped: 4



ANSWER CHOICES	RESPONSES	
Difficulty identifying and managing sepsis	0.00%	0
Lack of ICU availability	59.26%	16
Prefer to continue crystalloid support beyond 30mL/kg	29.63%	8
Unfamiliar/uncomfortable managing vasopressors	48.15%	13
Institution-specific policy regarding sepsis management	40.74%	11
Lack of central venous access	44.44%	12
Total Respondents: 27		

Appendix F

ANOVA Testing of Hyperlactatemia in Association with Provider Experience Level

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	3.085	1	3.085	3.044	.092[b]
	Residual	28.381	28	1.014		
	Total	31.467	29			

a. Dependent Variable: Lactate >4

b. Predictors: (Constant), How long have you been treating septic patients?

Appendix G

ANOVA Testing of Known Recent Infection with Provider Experience Level

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	3.225	1	3.225	3.209	.084[b]
	Residual	28.142	28	1.005		
	Total	31.367	29			

a. Dependent Variable: Known recent sepsis or bacteremia

b. Predictors: (Constant), How long have you been treating septic patients?

Appendix H

ANOVA Testing of MAP<60 with Provider Experience Level

ANOVA[a]

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	1.617	1	1.617	.989	.328[b]
	Residual	45.750	28	1.634		
	Total	47.367	29			

a. Dependent Variable: Map <60

b. Predictors: (Constant), How long have you been treating septic patients?