Successful Outcomes of Critically Ill Patients with Extreme Metabolic Acidosis Treated with Structured Approach: Case Series

Clinical Medicine Insights: Case Reports
Volume 14: 1–6
© The Author(s) 2021
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/11795476211025138

Sasa Dragic[1], Danica Momcicevic[1], Biljana Zlojutro[1], Milka Jandric[1], Tijana Kovacevic[2], Vlado Djajic[3], Ognjen Gajic[4] and Pedja Kovacevic[1]

[1]Medical Intensive Care Unit, University Clinical Centre of the Republic of Srpska, Bosnia and Herzegovina. [2]Clinical Pharmacy, University Clinical Centre of the Republic of Srpska, Bosnia and Herzegovina. [3]Management, University Clinical Centre of the Republic of Srpska, Bosnia and Herzegovina. [4]Mayo Clinic, Rochester, USA.

ABSTRACT

INTRODUCTION: Hydrogen ion concentration which is expressed as pH value is in human blood maintained in narrow physiological range (7.36-7.44 in arterial blood). This range is crucial for normal functioning of most biochemical reactions. Extreme acidosis with pH < 6.8 is incompatible with life, unless pathophysiologic process is rapidly reversed. Timely, standardized, and structured approach to assessment and management of extreme critical illness is essential to maximize the chances of patient's survival.

CASES: We present a series of 3 critically ill patients admitted to Medical intensive care unit (MICU) diagnosed with extreme metabolic acidosis (pH ⩽ 6.8). Each patient was treated using **C**hecklist for **E**arly **R**ecognition and **T**reatment of **A**cute **I**llness and I**N**jury (CERTAIN) which is a standard decision support tool in our MICU. Causes of extreme metabolic acidosis included hemorrhagic shock, sepsis, and acute renal failure and diabetic ketoacidosis. Rapid assessment, prompt resuscitation (IV fluids, vasopressors, mechanical ventilation, and renal replacement), and application of specific causal treatment led to positive outcomes in all 3 patients.

DISCUSSION: Medical physiology textbooks set the lower limit of pH value at which life is possible to 6.8. However, examples from clinical practice show that if adequate resuscitation measures are taken early in the acute phase of the disease, the biochemical cascade of reactions that are considered irreversible (at pH ⩽ 6.8) may be reversed after all.

CONCLUSION: Critical care approach to extreme metabolic acidosis is a prime example of applied clinical physiology where basic science and clinical practice connect. With these case series we show that timely and structured approach to critical illness shifts the boundaries of reversibility for some of the most severe physiologic derangements.

KEYWORDS: Acid-base status, acidosis, lactate, buffer

RECEIVED: September 26, 2020. **ACCEPTED:** May 26, 2021.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

CORRESPONDING AUTHOR: Sasa Dragic, Medical Intensive Care Unit, University Clinical Centre of the Republic of Srpska, Bosnia and Herzegovina.
Email: sasa.dragic@kc-bl.com

Introduction

Acid-base balance or hydrogen ion homeostasis (expressed as pH value) is crucial for normal functioning and metabolism of all cells, tissues, and organs. In human organism, acid-base balance is maintained keeping the pH value of arterial blood in narrow range of 7.36 to 7.44. Each oscillation of pH value outside of this range represents potential hazard for many essential metabolic and enzyme systems as well as transmembrane transport processes which in clinical sense can lead to cardiorespiratory failure.[1,2]

Physiological buffer systems along with lungs and kidneys try to prevent pH value oscillations outside the defined range and in that way enable normal functioning of all cells, tissues, and organs in human body.[3] However, these compensatory mechanisms are not always effective and sufficient, especially in acute illness and if resuscitation measures are not available.

One of these conditions include extreme acidosis for which we know that leads to functional disorders at molecular level and which clinically manifests in change of functioning of most organs and organ systems. There are various causes of severe metabolic acidosis but it is mostly seen in clinical disorders such as ketoacidosis, sepsis, and hypovolemia.[4]

Acutely, acidosis jeopardizes oxygenation, has depressive effect to heart contractility, causes arrhythmia and increase in pulmonary vascular resistance. Additionally it increases the chance of coagulopathy, leads to disturbance in thermoregulation. Vital proteins' configuration is altered in acidosis leading to its dysfunction. Severe acidosis can cause extremely resistant peripheral vasodilatation which requires administration of high doses of vasopressors. Possible cause of this might be decreased affinity of inotrope and vasopressor receptors.[5-7]

Patients with severe acid-base disorders require treatment in intensive care units with prompt reaction from critical care

physicians. It is essential to provide a rapid, structured assessment, and early adequate resuscitation to stop and reverse potentially fatal pathophysiological derangements in order to lower the mortality rate of patients presenting with extreme acidosis.

Case Series Report

We present 3 critically ill patients with severe metabolic acidosis characterized by different etiologies. Patients were initially admitted and treated in medical intensive care unit (MICU) of University Clinical Centre Republic of Srpska, where CERTAIN platform (**CERTAIN** = **C**hecklist for **E**arly **R**ecognition and **T**reatment of **A**cute **I**llness and I**N**jury) is used during admissions and daily rounds. CERTAIN platform is electronic tool developed by experts from *Mayo Clinic*, to serve as standardized approach in evaluation and treatment of acutely decompensated patients.[8,9] It is available in electronic and printed version as *CERTAIN Admission and Rounding Checklist (Appendix 1 and Appendix 2).*

Table 1 presents a structured overview of all 3 cases. Interpretation of clinical data along with laboratory, radiological and results of other diagnostic procedures is of great help in the rapid establishment of a working diagnosis and the most acceptable therapeutic modalities.

Clinical Observations, Initial Diagnostic and Treatment Approach: Resuscitation Measures and Outcome

Patient 1

Through clinical assessment of the patient we noted pale skin, hypotension, hypothermia and anuria. We learned about patient's hematemesis through heteroanamnesis. Test results revealed severe anemic syndrome (Hb 31 g/L) without coagulation cascade disorder. pH value was 6.78 and lactate level was 20.4 mmol/L. It was concluded that patient is in hypovolemic (hemorrhagic) shock and previously started resuscitation with oxygen (IV fluids, blood derivatives, vasopressors, haemostatic, and other symptomatic-supportive measures) was continued for 24 hours after which patient's vital functions were stabilized. Gastrointestinal endoscopy revealed huge amount of blood in patient's stomach without bleeding source visualization at that moment. On the third day of MICU hospitalization, it was decided to transfer the patient to gastroenterology ward where in further examination infiltrative change in stomach was found. Tissue sample of patient's stomach was taken for further histopathology analysis.

Patient 2

Through clinical assessment of the patient, we noted hypotension and anuria, along with changes in ECG in sense of bradycardia with high T waves. Patient has been suffering from rheumatoid arthritis and diabetes mellitus and has used insulin and methotrexate with folic acid regularly. Laboratory analysis revealed increased markers of inflammation, hyperkalemia (7.7 mmol/L), increased lactate levels (10.4 mmol/L), extremely increased urea and creatinine levels (45.5 mmol/L and 1245 μmol/L, respectively), with acidemia and pH value of 6.79. The urinary sediment analysis showed pathological findings. It was concluded that severe acidosis was caused by acute renal failure which was triggered by urosepsis. Resuscitation with oxygen, IV fluids, vasopressors, corticosteroids, wide spectrum antibiotics, and other symptomatic-supportive measures was started immediately. CVVHD was started and was continued for 24 hours along with all other resuscitation measures after which patient's heart rate finally stabilized. Vasopressor doses were initially decreased and then stopped. Patient's diuresis was regained. After 7 days of hospitalization in the MICU, patient's vital functions became stable. There was no need for further dialysis and we decided to transfer the patient to step down unit—hematology ward, due to evident decrease in values of all types of blood cells for further diagnostic evaluation. Blood smear analysis led to conclusion that methotrexate was the probable cause of hematologic disorder. After provision of adequate therapeutic measures, patient fully recovered, and was discharged from the hospital.

Patient 3

On admission patient's level of conciseness was determined (GCS 7) and painful abdomen was detected. Abdominal surgeon was consulted and urgent ultrasound and CT of patient's abdomen were performed, which both came back normal. Hence, acute intrabdominal and other surgical disorders were excluded. Through heteroanamnesis, it was found out that patent has had diabetes mellitus for many years. Laboratory analysis of patient's blood revealed leukocytosis, pH value of 6.65, bicarbonate level of 1.8 mmol/L and lactate level of 4.2 mmol/L. Extremely high values of glucose were detected, despite the fact that short acting insulin was self-administered by patient at home shortly before arrival to hospital. Due to disturbed conciseness and inadequately functioning airway, patient was intubated and controlled mechanical ventilation was started. Diabetic ketoacidosis was suspected, triggered most probably by infection with unknown locus. Resuscitation was started immediately with IV fluids, vasopressor, empirical wide-spectrum antimicrobial therapy, continuous IV infusion of insulin, IV electrolytes, and other symptomatic and supportive measures which eventually led to regulation of acid-base status and clinical recovery of the patient. On the fourth day of MICU hospitalization, it was decided to transfer the patient to step down unit -endocrinology ward. In the next few days, adequate glycemic control was achieved, and patient was discharged from the hospital.

Table 1. Case series presentation using structured approach.

TYPE OF DATA	RESULTS		
	PATIENT 1	PATIENT 2	PATIENT 3
Reason for admission	Hemorrhagic shock caused by gastrointestinal bleeding	Urosepsis with acute renal failure	Diabetic ketoacidosis (plus probable infection with unknown locus)
Sex (♂/♀)	♂	♀	♀
Age (years)	72	68	40
Height/weight (cm/kg)	178/80	170/84	180/70
HR (beat per minute)	100	48	120
BP (mmHg)	85/50	80/50	140/90
RR (per minute)	26	28	36
Temperature (°C)	33.5	37.1	36.2
UO (ml/h)	0	0	450
Pain intensity scale (0-10)	0	0	7
A (airway)	Normal	Normal	Compromised airway
B (breathing)	Increased respiratory work	Increased respiratory work	Increased respiratory work
C (circulation)	Mottling	Bradycardia	Sinus tachycardia
D (disability)	Fulfills verbal orders	Fulfills verbal orders	Responds to pain stimuli
E (exposure)	Hematemesis	No visible signs	Distended, painful abdomen
WBC ($\times 10^9$/L)	27.9	11.7	23.9
Hb (g/L)	31	111	128
Plt ($\times 10^9$/L)	430	269	445
INR	1.36	1.12	0.92
Glu (mmol/L)	12.6	1.6	9.2
Na (mmol/l)	140	130	144
K (mmol/L)	5.3	7.7	144
Ca (mmol/L)	2.08	1.83	1.79
BilT/BilD (μmol/L)	4.6/1.7	5.3/3.3	3.2/2.3
Urea (mol/L)	18.5	45.5	3.5
Cr (μmol/L)	110	1245	90
pH	6.78	6.792	6.659
pCO_2 (kPa)	3.57	6.02	2.21
pO_2 (kPa)	4.44	5.5	11.6
HCO_3 (mmol/L)	4.3	6.5	1.8
sO_2 (%)	29.7	49	90.2
Lac (mmol/L)	20.1	10.4	4.2
Medical history	Diabetes mellitus type 2	Rheumatoid arthritis	Diabetes mellitus type 1
	Ischemic cardiomyopathy	Diabetes mellitus type 2	
		Obesity	

(Continued)

Table 1. (Continued)

TYPE OF DATA	RESULTS		
	PATIENT 1	PATIENT 2	PATIENT 3
ECG (pathological finding)	Left branch block	Left branch block	Sinus tachycardia up to 120 bpm
US (pathological finding)	Collapsible inferior vena cava	Collapsible inferior vena cava	Collapsible inferior vena cava
CXR (pathological finding)	Normal	Normal	Normal
CT (pathological finding)	Not performed	Not performed	Thorax and abdomen- normal
Other	Esophagogastroduodenoscopy bleeding	None	None
Interventions	Oxygen therapy (mask); crystalloid infusion (5 L); PPI (pantoprazole); blood transfusion (6 pcs of RBCs and 3 fresh frozen plasmas); tranexamic acid; vasopressor (noradrenalin IV continuously during 5 h); antibiotics (meropenem and metronidazole); IV insulin; IV electrolytes	Oxygen therapy (mask); crystalloid infusion (6 L); vasopressor (noradrenalin IV continuously during 8 h); IV insulin; antibiotics (azithromycin and ciprofloxacin); corticosteroid (hydrocortisone); PPI (pantoprazole); IV electrolytes; VVHDF (due to metabolic acidosis)	Sedation (Propofol continuous IV infusion) + myorelaxant (atracurium continuous IV infusion) due to intubation and mechanical ventilation; crystalloid infusion (5 L); sodium bicarbonate; IV insulin; antibiotics (ceftriaxone and azithromycin; PPI (pantoprazole); thromboprophylaxis (UFH); IV electrolytes

Discussion

Medical physiology textbooks set the lower limit of pH value at which life is possible to 6.8. However, examples from clinical practice show that if adequate resuscitation measures are provided early in the acute phase of the disease, the biochemical cascade of reactions that were considered irreversible at some point (at pH $\leqslant$ 6.8) may be reversed after all.[10,11] Case series presented here, confirm these statements.

In the first case report, patient experienced hypovolemic (hemorrhagic) shock. It is well known that untreated hypovolemic shock leads to severe acidosis, and that only 1 out of 3 patients survives initial resuscitation.[10,12] Mortality rate in acidosis caused by hemorrhagic shock is 86% as shown in clinical studies with small size samples.[11] It is considered that providing fast resuscitation measures to patient with severe hemorrhagic shock and metabolic acidosis can lead to patient's survival. It is proven that presence of multiorgan disfunction impacts survival rate. Case report found in the literature shows successful treatment of polytraumatized patient in hemorrhagic shock with metabolic acidosis and pH value of 6.5.[13] In situations like this, acidosis is always triggered by tissue hypoperfusion, and without oxygen supplementation, conditions for anabolic metabolism and excessive lactate production are met. Identical pathophysiological mechanism is seen in patient case we described. Lactate level is always in correlation to hypoperfusion severity; on the other side lactate level is biomarker of hemorrhagic shock. Fast volume and blood cells repletion along with oxygen therapy was crucial in resuscitation of patient presented in this case report. In addition, correction of severe acidosis (and hypothermia) is important for adequate coagulation and hemostasis.[14]

Second case report describes patient with acute renal failure most likely triggered by sepsis. Kidneys are frequently affected by impaired oxygen balance due to impaired perfusion in all forms of shock. Hypoperfusion may also lead to increase in serum creatinine and blood urea nitrogen levels, which are the most commonly used biomarkers of renal function.

These findings along with detected metabolic acidosis were dominant in second patient case. Sepsis induced peripheral vasodilatation, fall in arterial pressure, and renal hypoperfusion in patient causing acute renal failure and expression of its signs: hyperkalemia, increase in level of hyperosmolar compounds and acid-base disorder. Patient's organism was pulled into vicious circle where treatment usually becomes ineffective due to severe acidosis. Both lactic acidosis and acute renal failure contributed to development of extreme metabolic acidosis in this patient.[15] Renal replacement therapy is necessary when uremic symptoms develop with excess extracellular volume, hyperkalemia, or metabolic acidosis refractory to medical therapy. Continuous renal replacement therapies can be used for fluid removal (ultrafiltration) or solute removal (dyalisis, hemofiltration, hemodiafiltration). An appropriate selection depends on the circumstances around the individual patient (especially his or her hemodynamic status).[16] Only after starting continuous veno-venous hemodiafiltration (CVVHDF) the patient's condition started to improve.

Third case report describes a patient with classical diabetic ketoacidosis which represents acute metabolic complication of

diabetes mellitus characterized by hyperglycemia, hyperketonemia, and metabolic acidosis. Hyperglycemia leads to osmotic diuresis and is much more often seen in diabetes mellitus type I. It is manifested with nausea, vomiting, and abdominal pain which was dominant symptom in presented patient, and if fast resuscitations measures are not applied, patient's condition can complicate to brain edema, coma and death.[17] Diagnosis is made due to presence of hyperketonemia, metabolic acidosis with anion gap and hyperglycemia. Treatment includes volume resuscitation, insulin administration and hypokalemia prevention. Insulin normally inhibits ketogenesis, hence in lack of insulin ketone products are created which can lead to metabolic acidosis.[18] Elevated lactate levels are often seen in diabetic ketoacidosis, and those are consequence of inadequate tissue perfusion (due to decrease in intravascular volume, presence of micro- and macroangiopathy, increase in glycolyzed hemoglobin, and abnormal platelet function). Further, hypoxemia stimulates process of anaerobic glycolysis where pyruvate is metabolized to lactate along with 2 molecules of adenosine triphosphate (ATP).[19,20] In general, diabetic acidosis is associated with higher survival rates compared to other causes of extreme metabolic acidosis (pH $<$ 6.8).

Conclusion

Blood gas analysis along with acid-base status interpretation represent example of connection between basic physiology science and clinical practice.

These clinical practice examples can serve to show that development of modern intensive care medicine with adequately trained critical care staff, adequate space, and equipment, and the structured approach to critical illness during golden hours shifts the boundaries of reversibility of even extreme acute physiological impairments.

Regardless of the etiology of severe metabolic acidosis, it has been shown that timely initiation of adequate resuscitation procedures along with other specific and symptomatic measures is a key link in the successful treatment of these patients.

Author Contributions

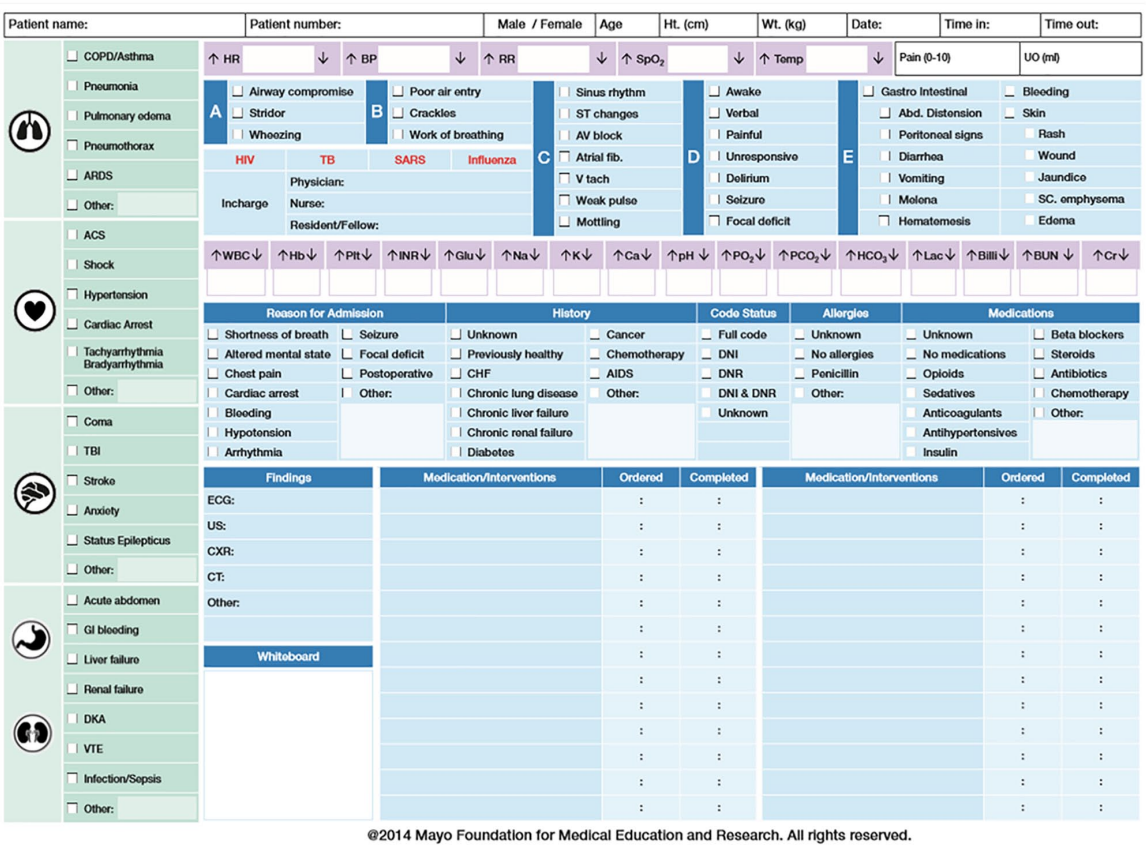
Sasa Dragic, Danica Momcicevic, Biljana Zlojutro, Milka Jandric and Tijana Kovacevic participated in the treatment of all patients and wrote this article. Vlado Djajic, Ognjen Gajic and Pedja Kovacevic read and approved the final manuscript.

Patient Consent Confirmation Statement

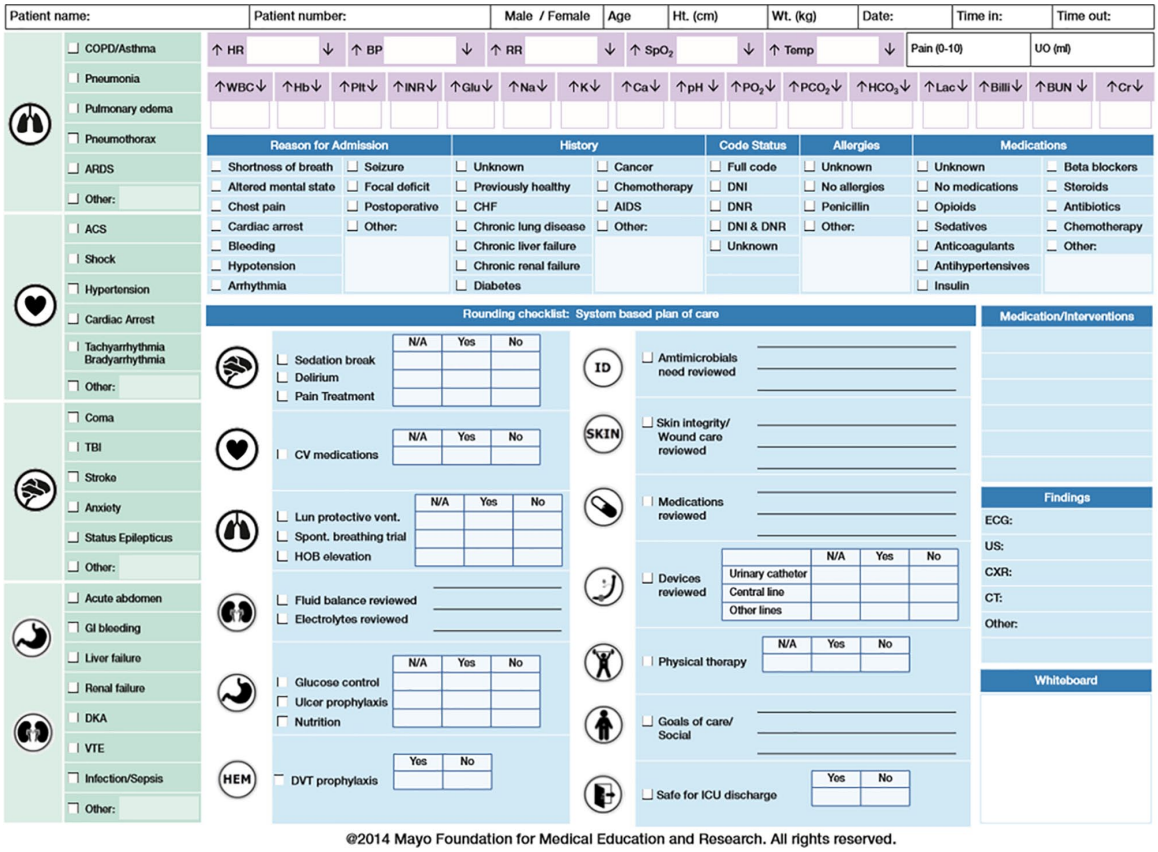
Appropriate consent to publish case details was obtained from the patients.

REFERENCES

1. Berend K, De Vries AP, Gans RO. Physiological approach to assessment of acid-base disturbances. *N Engl Med*. 2014;371:1434-1445.
2. Berend K. Acid-base pathophysiology after 130 years: confusing, irrational and controversial. *J Nephrol*. 2013;26:254-265.
3. Mitchell JH, Wildenthal K, Johnson RL Jr. The effects of acid-base disturbances on cardiovascular and pulmonary function. *Kidney Int*. 1972;1:375-389.
4. Lim S. Metabolic acidosis. *Acta Med Indones*. 2007;39:145-150.
5. Schotola H, Toischer K, Popov AF, et al. Mild metabolic acidosis impairs the beta-adrenergic response in isolated human failing myocardium. *Crit Care*. 2012;16:R153.
6. Kim SI, Shoemaker WC. Role of the acidosis in the development of increased pulmonary vascular resistance and shock lung in experimental hemorrhagic shock. *Surgery*. 1973;73:723-729.
7. Smith SA, Livingston MH, Merritt NH. Early coagulopathy and metabolic acidosis predict transfusion of packed red blood cells in pediatric trauma patients. *J Pediatr Surg*. 2016;51:848-852.
8. Vukoja M, Kashyap R, Gavrilovic S, Dong Y, Kilickaya O, Gajic O. Checklist for early recognition and treatment of acute illness: international collaboration to improve critical care practice. *World J Crit Care Med*. 2015;4:55-61.
9. Sevilla-Berrios R, O'Horo JC, Schmickl CN, et al. Prompting with electronic checklist improves clinician performance in medical emergencies: a high-fidelity simulation study. *Int J Emerg Med*. 2018;11:26.
10. Ross SW, Thomas BW, Christmas AB, Cunningham KW, Sing RF. Returning from the acidotic abyss: mortality in trauma patient with pH$\leqslant$7.0. *Am J Surg*. 2017;214:1067-1072.
11. Allyn J, Vandroux D, Jabot J, et al. Prognosis of patients presenting extreme acidosis (pH$<$7) on admission to intensive care unit. *J Crit Care*. 2016:31:243-248.
12. Caputo N, Summersgill A, Fraser R, Kanter M. 175 determining the utility of metabolic acidosis in trauma patients. *Ann Emerg Med*. 2013;62:S66.
13. Balmecada A, Arora S, Sondheimer I, Hollon MM. Resuscitation from pH of 6.5: a case report and review of patophysiology and management of extreme acidosis from hypovolemic shock after trauma. *J Trauma Inj*. 2019;32:238-242.
14. Shields DW, Crowley TP. Current concepts, which effect outcome following major hemorrhage. *J Emerg Trauma Shock*. 2014;7:20-24.
15. Suetrong B, Walley KR. Lactic acidosis in sepsis: it's all anaerobic: implication for diagnosis and management. *Chest*. 2016;149:252-261.
16. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO: clinical practice guideline for acute kidney injury. *Kidney Int Suppl*. 2012;2:1-138.
17. Kitabchi AE, Umpierrez GE, Miles JM, et al. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care*. 2009;32:1335-1343.
18. Feenstra RA, Kiewiet MKP, Boerma EC, ter Avest E. Lactic acidosis in diabetic ketoacidosis. *BMJ Case Rep*. 2014;2014:bcr2014203594.
19. Fuluop M, Hoberman HD, Rascoff JH, et al. Lactic acidosis in diabetic patient. *Arch Intern Med*. 1976;136:987-990.
20. Bakker J, Gris P, Coffernils M, et al. Serial blood lactate levels can predict the development of multiorgan failure following septic shock. *Am J Surg*. 1996;171:221-226.



Appendix 1. CERTAIN – admission checklist.



Appendix 2. CERTAIN – rounding checklist.