

## PREVALENCE, PATTERN AND CLINICAL OUTCOME OF CIRCULATORY SHOCK IN CRITICALLY ILL PATIENTS IN MEDICAL ICU

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### ABSTRACT

**Background:** To study the epidemiology of circulatory shock secondly to assess different pattern of circulatory shock among adult critically ill patients admitted to medical ICU of internal medicine department Zagazig University during the study period and finally to study the clinical outcome (morbidity and mortality) of different pattern of circulatory shock.

**Methods and subjects:** The current Cross-sectional cohort study had been carried out on 694 patients with circulatory shock who were admitted in medical ICU with criteria of peripheral circulatory failure. The included patients were subdivided into three groups according to the provisional and definitive diagnosis of type of circulatory shock depending on CVP, echocardiography, cardiac output and laboratory investigations as follow: Group1: hypovolemic shock group ,Group 2: cardiogenic shock group and Group 3: septic shock group. All patients were subjected to thorough medical and clinical history taking and full clinical assessment. Blood samples were withdrawn for routine investigations (Complete blood count, Kidney function tests, Liver function tests, CRP, INR, Arterial blood gases (ABG), Mean saturation of central venous oxygen (ScvO<sub>2</sub>) and serum lactate. Shock severity was assessed by using APACHE IV score and SOFA score.

**Results:** The frequency of circulatory shock patients is 13.9% per year. Hypovolemic shock was the major cause of circulatory failure in the studied population followed by septic shock and finally cardiogenic shock. The severity assessment parameters including APPACHE IV score , SOFA score, length of hospital stay and GCS were statically significant difference among the three studied groups, with significant increase in APPACHE IV score and SOFA score in cardiogenic group. APPACHE IV score and SOFA score were significant independent predictor of survival. The outcome measures of our populations during their ICU stay and after discharge to the medical words shows that mortality increase progressively with increase the length of ICU stay, there was significant difference in survival among the three groups, the most favorable outcome is hypovolemic group, and the worst was observed in the cardiogenic shock group.

**Conclusions:** Circulatory shock is a life threatening condition associated with high mortality so early recognition and early intervention will decrease morbidity and mortality in critically ill patients. CVP, echocardiography and laboratory investigations especially serum lactate and SCVO<sub>2</sub> are easy, reliable and available in all emergency departments. All can help in early diagnosis of type of circulatory shock. Calculation of APPACHE IV score and SOFA score were easy and reliable which potentially allow one to diagnose life-threatening condition and treat them before laboratory results are back.

**Key words:** Circulatory Shock, medical ICU

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### INTRODUCTION

Circulatory shock is a life threatening condition associated with high mortality characterized by inadequate delivery of oxygen and nutrients to vital organs relative to their metabolic demand. Inadequate oxygen delivery typically results from poor tissue perfusion but occasionally, may be also caused by an increase in metabolic demand [1].

In critically ill patients, tissue hypoxia is due to inadequate or disordered regional distribution of blood flow both between and within organs. Inadequate perfusion leads to the generation of lactate and hydrogen ions

which spill over into the bloodstream, leading to the biological profile of lactic acidosis [2].

The effects of oxygen deprivation are initially reversible, but rapidly become irreversible. The result is sequential cell death, end-organ damage, multi-system organ shock, and death. This highlights the importance of prompt recognition and reversal of shock [3].

Despite the high prevalence and morbidity of shock, the lack of a widely accepted definition and clear diagnostic criteria have limited the development of robust epidemiologic data. Estimates suggest that more than 1.2 million emergency

department visits annually are for patients in shock. Mortality for patients in shock varies depending on the cause, but common causes of shock including sepsis, trauma, and cardiac shock have mortality ranging from 20% to 50% [4].

The classification of shock based mainly on the discharge diagnosis or death diagnosis. The combination of a clinical infection, the presence of systemic inflammatory response syndrome (SIRS) and acute circulatory shock were defined septic shock. On other hand, the patients lost more than 30% total blood volume in 24 hours or lost more than 15% total blood volume in 3 hours with acute circulatory shock was defined hypovolemic shock. The patients who have foundational heart disease and acute circulatory shock, but without infection causes and acute blood loss reasons was defined cardiogenic shock [5].

Emergency providers are frequently presented with the undifferentiated patient and must be intimately familiar with the elements of history, physical examination, and diagnostic testing that may suggest early shock, before the onset of significant organ dysfunction [6].

Vital-sign abnormalities have long been the cornerstone of shock recognition. Traditionally, a patient was deemed to be in shock when tachycardic, tachypneic, and possessing a systolic blood pressure (SBP) less than 90 mm Hg. Also calculation of the shock index (the heart rate divided by the SBP) can improve the detection of critically ill patients compared to HR and BP alone [7].

In addition to vital signs, which focus on the cardiac and respiratory systems, other physical examination findings are helpful in the recognition of tissue hypoperfusion. Altered mental status, poor skin perfusion, and oliguria are markers of decreased end-organ perfusion and have been found to be independent predictors of 30-day mortality in patients with cardiogenic shock [8].

Internationally endorsed clinical guidelines recommend using CVP as the end point of fluid resuscitation. The early goal-directed therapy studying based on the surviving sepsis campaign guidelines for management of severe sepsis and the ARDS

net fluid management trial support using CVP to guide fluid therapy [9].

Early recognition and correspondingly early intervention before the onset of multiple organ dysfunction have been demonstrated to decrease morbidity and mortality in critically ill patients. Goal-directed therapy, attempted for years in the intensive care unit (ICU) with variable results, when implemented within the first 6 hours of presentation to the ED improved absolute mortality by 16% [10].

## PATIENTS AND METHODS

**Study design:** The current cross sectional study had been conducted in the period extending from January to December 2017 in Medical Intensive Care Unit of the Internal Medicine Department Zagazig University Hospitals, Egypt.

**Patients:** Out of 4997 patients who were admitted to medical ICU in the period extending from January to December 2017. 737 patients who were admitted with circulatory shock. Out of them 43 patients were excluded due to missed data and the remaining 694 patients were included in the study. 308 of them were males and 386 patients were females their ages ranged from 38 year to 76 year with mean of 55 year .

The diagnosis of peripheral circulatory failure was based on the presence of the following criteria: Arterial hypotension , defined as systolic blood pressure of <90 mmHg or a decrease of < 40 mmHg from baseline (although this was not always present), narrow pulse pressure that is indicative of reduced stroke volume (Ceconi et al., 2014). Cold, clammy and blue, pale or discolored skin (The peripheral window). Decreased urine output: < 0.5 mL/kg/h (The renal window) and altered mental status that characterized by obtundation, disorientation and confusion (The neurologic window) (Van Genderen et al., 2013).

The included patients were subdivided into three groups according to the provisional and definitive diagnosis of type of circulatory shock (depending on CVP, echocardiography, cardiac output and laboratory investigations) as follow:

**Group 1: hypovolemic shock group:** Included 357 patients, 154 of them were males and the remaining 203 were females, their

ages were range from 38–70 years with a mean of (50.5±7.7y). All patients had low CVP and low COP diagnosed by Echo .The causes of hypovolemia were blood loss (hematemesis, melena), fluid loss as perfuse vomiting and / or diarrhea.

**Group 2: cardiogenic shock group:** Included 84 patients, 28 of them were males and the remaining 56 were females, their ages ranged from 50–67 years with a mean of (58.6±4.1y) on admission. All patients had high CVP and low COP by Echo. Cardiogenic shock was due to loss of contractility (myocardial infarction and its complications), impaired diastolic filling, abnormal rate or rhythm; or obstruction to flow that is due to valvular conditions, pulmonary embolus, or tamponade.

**Group 3: septic shock group:** Included 253 patients, 126 of them were males and the remaining 127 were females; their ages ranged from 40–76 years with a mean of (57.9±9.9y). Those Patients had clinical signs of SIRS with low or normal CVP and normal or even increased COP (warm shock) in the beginning as sepsis progresses, stroke volume and cardiac output fall. The patients begin to manifest the signs of poor perfusion and delayed capillary refill (cold shock). Sepsis mostly due to serious gastrointestinal , respiratory or urinary tract infections.

All patients were subjected to thorough medical and clinical history taking and full clinical assessment. Blood samples were withdrawn for routine investigations (Complete blood count, Kidney function tests, Liver function tests, random blood sugar (RBS), urine and stool analysis, CRP, INR, Prothrombin time (PT), Partial Thromboplastin Time (PTT), Arterial blood gases (ABG), Mean saturation of central venous oxygen (ScvO<sub>2</sub>) from CVP and Serum lactate.

Severity assessment by using the most commonly used scoring systems in patients with critical illness in ICU including APACHE IV score at time of admission and SOFA score (Sequential Organ Failure Assessment score) to determine the extent of a patient's organ function or rate of failure during the stay in an intensive care unit (ICU).

**Exclusion criteria:** Any patient with missing data.

**Ethical clearance:** Written Informed consent was taken from the first degree relative to participate in the study. Approval for performing the study was obtained from internal medicine and medical biochemistry departments, Zagazig University Hospitals after taking Institutional Review Board (IRB) approval (IRB:1386/1-4-2014).

#### **Statistical analysis**

The collected data were statistically analyzed using SPSS program (Statistical Package for Social Science) version 20 .Data were tested for normal distribution using the Shapiro Walk test. Chi square test ( $\chi^2$ ) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as mean  $\pm$  SD (Standard deviation) for parametric and median and range for non-parametric data . Independent T test and Mann Whitney test were used to calculate difference between quantitative variables in two groups for parametric and non-parametric variables respectively. One-way ANOVA F-test and Kruskal-Wallis Test were used to calculate difference between quantitative variables in more than two groups in normally normal and non-parametric variables respectively. Post hoc test for multiple comparisons was done by using LSD and Dunn's test parametric and non-parametric variables respectively Spearman's correlation tests were used for correlating non-parametric variables.

Survival analysis Kaplan and Meier method used to estimate overall survival and log rank test compared survival curves (P value was considered significant at  $\leq 0.05$  levels. All statistical comparisons were two tailed with significance Level of P-value  $\leq 0.05$  indicates significant,  $p < 0.001$  indicates highly significant difference while,  $P > 0.05$  indicates Non-significant difference.

#### **RESULTS**

**Table (1)** shows that out of 4997 patients admitted to medical ICU during one year, only 694 patients had circulatory shock. So the incidence of circulatory shock patients is 13.9% in one year.

**Table (2)** shows the frequency and the percentage distribution of the circulatory

shock patients, the highest frequency of patients developed circulatory shock was hypovolemic shock (51.4%) followed by septic shock (36.5%) and the lowest frequency was cardiogenic shock (12.1%).

**Table (3)** shows Severity Assessment parameters among the studied patient. SOFA score range from 4 to 29 with median 15, APPACHE IV score range from 45 to 140 with median 88, the length of hospital stay ranged from 1 day to 16 with median 6 days and GCS range from 4 to 15 with median 12 among the studied patients.

**Table (4)** shows the frequency and the percentage distribution of the circulatory shock patients according to their clinical outcome. Poor outcome as the highest frequency observed in death rate (39.3%), while improved patients frequency was (32.4%), and the lowest frequency was complicated patients (28.2%).

**Table (5)** shows the frequency and distribution among the three studied groups as

regard clinical outcome as the highest frequency of death rate (58.3%) and complicated outcome (41.7%) was among cardiogenic shock group and the highest frequency of improved Patients (49.0%) was among hypovolemic shock group. lowest frequency of death rate (33.3%) and complicated outcome (17.6%) was among hypovolemic shock group, and lowest frequency of improved Patients (19.8%) among septic shock group.

**Table (6)** shows that only SOFA score and APPACHE IV score ( $p < 0.001$ ) were independent risk factors in hospital mortality among the studied patients who admitted with circulatory shock.

**Table (7)** shows that SOFA score ( $p < 0.001$ ) were independent risk factors in hospital mortality among the septic group who admitted with circulatory shock compared to both hypovolemic and cardiogenic shock groups.

**Table (1): Frequency and Percentage distribution of patients with circulatory shock in the present study during one year.**

	Frequency (n)	Percentage (%)
Total patients	4997	100
Circulatory shock patients	694	13.9

**Table (2): Frequency and Percentage distribution of the circulatory shock patients according to pattern of shock.**

Parameters	Frequency	Percentage
Pattern of shock	Hypovolemic	357 (51.4%)
	Cardiogenic	84 (12.1%)
	Septic	253 (36.5%)

**Table (3): Severity Assessment parameters of the studied patients with circulatory shock.**

Parameters	Median (range)
SOFA	15 (4-29)
APPACHE	88 (45-140)
LOS, days Median (range)	6 (1-16)
GCS	12 (4-15)

**Table (4): Frequency and Percentage distribution of the studied patients with circulatory shock as regard clinical outcome.**

Parameters		Frequency	Percentage
Outcome	Death	273	(39.3%)
	Complicated	196	(28.2%)
	Improved	225	(32.4%)

**Table (5): Comparison of Frequency and Percentage distribution among the studied groups according to clinical outcome as regard to different pattern of shock.**

		Pattern of shock			T	P
		Hypovolemic	Cardiogenic	Septic		
		N=357	N=84	N=253		
Outcome	Death	119 (33.3%)	49 (58.3%)	105 (41.5%)	135.5	<0.001
	Complicated	63 (17.6%)	35 (41.7%)	98 (38.7%)		
	Improved	175 (49.0%)	0 (0.0%)	50 (19.8%)		

**Table (6): Multivariate COX regression analysis of severity assesment parameters on overall Survival rate of patients with circulatory shock.**

	B	SE	HR	95.0% CI for HR		Sig.
				Lower	Upper	
SOFA	0.07	0.02	1.07	1.041	1.107	<0.001
APPACHE	0.03	0.01	1.03	1.024	1.045	<0.001
GCS	9.38	26.25	1.7	0.007	2.6	0.721

**Table (7): Multivariate COX regression analysis of overall Survival rate of the hospitalized ICUs patients in relation to other studied parameters in each group.**

Diagnosis	Variable	$\beta$	SE	HR	95.0% CI for HR		Sig.
					Lower	Upper	
Hypovolemic	SOFA	0.170	0.031	1.185	1.116	1.259	0.06
	APPACH	0.011	0.007	1.011	0.997	1.025	<0.001
Cardiogenic	SOFA	-0.034	0.037	0.967	0.899	1.040	0.362
	APPACH	0.038	0.040	1.039	0.959	1.124	<0.001
Septic	SOFA	0.084	0.023	1.088	1.040	1.138	<0.001
	APPACH	.047	0.007	1.048	1.033	1.062	<0.001

## DISCUSSION

Circulatory shock is a life threatening condition associated with high mortality characterized by inadequate delivery of oxygen and nutrients to vital organs relative to their metabolic demand. Inadequate oxygen delivery typically results from poor tissue perfusion but occasionally, may be also caused by an increase in metabolic demand [1].

Up to one-third of patients admitted to the ICU are in circulatory shock, and early recognition of the condition is vital if subsequent tissue injuries are to be avoided. Shock can be categorized according to the underlying cause, including septic shock, cardiogenic shock, anaphylactic shock and shock associated with burns, trauma and hemorrhage [11].

Early recognition and correspondingly early intervention before the onset of multiple organ dysfunctions have been demonstrated to decrease morbidity and mortality in critically ill patients. Goal-directed therapy, attempted for years in the intensive care unit (ICU) with variable results, when implemented within the first 6 hours of presentation to the ED improved absolute mortality by 16% [12].

This study was conducted to evaluate the epidemiology of circulatory shock and its different pattern among adult critically ill patients admitted to medical ICU of internal medicine department Zagazig University during the study period, and the clinical outcome (morbidity and mortality) of different pattern of circulatory shock. This Cross-sectional cohort study had been carried out in our medical ICU of internal medicine department in the period extending from January to December 2017 in the period of twelve months. Out of 737 patients who were included in this study 43 patients were excluded due to missed data and the remaining 694 patients were included in the study. 308 of them were male and 386 patients were female, their ages were ranged from 38 year to 76 year with mean of 55 year.

On admission all patients diagnosed as peripheral circulatory failure was based on presence of the following criteria: Arterial hypotension, narrow pulse pressure, Cold, clammy and blue and or pale skin, Decreased

urine output: < 0.5 mL/kg/h, and altered mental status that characterized by obtundation, disorientation and confusion [13].

The included patients were subdivided into three groups according to the provisional and definitive diagnosis of type of circulatory shock (depending on CVP, echocardiography, cardiac output and laboratory investigations) (**Cheryl and Keith, 2003**) as follow: Group 1 hypovolemic shock group all patients had low CVP and low COP, Group 2: cardiogenic shock group all patients had high CVP and low COP and Group 3: septic shock group Those Patients had clinical signs of SIRS with low or normal CVP and normal COP or even increased in the beginning as sepsis progresses cardiac output fall [14].

According to demographic results of our study the percentage of female was higher than male with no statically significant difference among the three studied groups. In addition there was significant difference among different groups concerning age and these differences in age distribution between different groups of the study was due to randomization in collection of our patients.

We observed that hypovolemic shock was the major cause of circulatory failure in the studied population (51.4%) followed by septic shock (36.5%) and finally cardiogenic shock (12.1%). This could be explained by the fact that, in most of our patients admitted with hypovolemia the main etiology was upper GIT bleeding as complication of portal hypertension and liver cirrhosis due to chronic viral hepatitis infection or schistosomal liver disease or the combination of both(mixed). Egypt has the highest prevalence of HCV infection in the whole world **Gomaa et al. (2017)** and complications of schistosomal liver disease and its treatment still represents a major health burden among the Egyptian population [15].

Most of western epidemiological studies found that septic shock is the main cause of circulatory failure in patients admitted to ICU, however septic shock comes next in our study, but still represents major sector of the studied population (36.5%). Sepsis and septic shock are more prevalent in the sector of population with low socio-economic levels. This is a fact in both the

developing and developed countries **Babaev et al. (2005)**. Factors includes low income, difficult to access to medical care facilities, illiteracy, delay in diagnosis and the late referral to intensive care units. Cardiogenic shock (17 %), mostly as a complication of acute coronary syndrome and MI represents the lowest prevalence among patients with circulatory failure admitted to ICU. Similar percent was documented in several studies of **Babaev et al. (2005)** and **Awad et al. (2013)** [16, 17].

Clinical parameters including both heart rate, respiratory rate, and CVP differed significantly between our three studied groups. All clinical parameters were higher in the septic shock group compared to other two groups. **Singer et al. (2016)** state that all shocked patients generally have tachypnea and tachycardia and mostly hypotension, while **Soller et al. (2008)** and **van Genderen et al. (2013)** suggested that the presence of low blood pressure should not be a prerequisite for defining shock as decrease cardiac output is associated with significant vasoconstriction, leading to decreased peripheral perfusion to maintain arterial pressure [18, 19, 20].

This implies the importance of assessment of physiological parameters, including airway, breathing, and circulation in every patient presented with acute circulatory failure. The diagnosis must based on combination of clinical, hemodynamic and biochemical signs **Vincent et al. (2012)** [21].

In our study there was statistically significant different in the laboratory parameters including PH, HCO<sub>3</sub>, serum lactate among the three studied groups these results emphasized by the importance of ABG, serum lactate as the same as the general condition of the patients **Kolte et al. (2014)** and **Shapiro et al. (2005)** who state that serum lactate is the best serum marker for tissue perfusion and a base deficit is also an important marker to follow during resuscitation of a patient from shock [9, 22].

Furthermore, there was statically significant difference in the central venous oxygen saturation (SCVO<sub>2</sub>) among the three studied groups, Low ScVO<sub>2</sub> (<70 %) indicates an inadequacy of oxygen transport

especially in the context of hyperlactatemia and poor outcome, we aimed at increasing the ScVO<sub>2</sub> to >70 % to get better outcome. This was supported by **Jones et al. (2010)** and **Rivers et al. (2001)** [23, 24].

We found that the severity assessment parameters including APPACHE IV score, SOFA score, length of hospital stay and GCS were statically significant difference among the three studied groups, with significant increase in APPACHE IV score and SOFA score among cardiogenic group compared to both septic and hypovolemic shock groups.

In the current study, the multivariate logistic regression model for hospital survival indicated that each APPACHE IV score and SOFA score were a significant independent predictor (p<0.001) of survival this have been reinforced by **Ferreira et al. (2001)** who asses that the severity of SOFA score as a contributor to mortality, while APPACHE IV score and SOFA score were significant independent predictor of survival (p<0.001) in septic shock group as result of the extent of a patient's organ function or rate of failure during the stay in an intensive care unit (ICU) which more common with sepsis this supported by **Ferreira et al., (2001)** [25].

We studied the outcome measures of our cohort populations during sixteen days of their ICU stay and after discharge to the medical words. Mortality increase progressively with increase the length of ICU stay, there was significant difference in survival among the three groups, with the most favorable outcome is hypovolemic group(49%) this agree with **Irwin et al. (2003)** who reported that Hypovolemic shock is readily treatable and respond well to medical therapy followed by septic group (19.8%). The worst outcome was observed in the cardiogenic group. This could be explained by the fact that most of patients included in the cardiogenic group were presented either in the state of post arrest or with severe complications. Patients with acute coronary syndrome who presents early are usually admitted to the coronary care unit for emergency PCI or thrombolysis, while the patients with complications and post-arrest patients are usually admitted to our internal

medicine ICU **Irwin et al. (2003)** and **Hamon et al. (2008)** [26, 27].

### CONCLUSION

Circulatory shock is a life threatening condition associated with high mortality so early recognition and early intervention will decrease morbidity and mortality in critically ill patients. CVP, echocardiography, cardiac output and laboratory investigations especially serum lactate and SCVO<sub>2</sub> are easy, reliable and available in all emergency departments. All can help in early diagnosis of type of circulatory shock. Calculation of APACHE IV score and SOFA score were easy and reliable which potentially allow one to diagnose life-threatening condition and treat them before laboratory results are back. Therefore correction of acidosis, hyperlactemia and accompanying low SCVO<sub>2</sub> must be as early as possible.

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