INCIDENCE AND PROGNOSTIC IMPACT OF NEW-ONSET ATRIAL FIBRILLATION IN PATIENTS WITH SEPTIC SHOCK

Megahed M M[1], Elsayed M M[1] and *Abdelaziz R R[2]

[1]Critical Care Medicine, Faculty of Medicine, University of Alexandria.
[2]Ministry of Health Egypt, Department of Critical Care
***Corresponding** Email: ramyryan@yahoo.com

ABSTRACT

Introduction: Since data regarding new-onset atrial fibrillation (AF) in septic shock patients are scarce, the purpose of the present study was to evaluate the incidence and prognostic impact of new-onset AF in this patient group.
Methods: prospectively studied the incidence of new-onset AF in 50 patients suffering from septic shock admitted consecutively to critical care units in the main Alexandria university hospital during a 6 month period from 1st October 2013 till the end of March 2014 and to evaluate its prognostic impact.
Results: During the study period, 63 patients were admitted to the ICU with septic shock, of which 13 patients were excluded from further analysis due to pre-existing chronic or intermittent AF. In remaining 50 patients divided into 2 groups Group I [septic shock with AF] & Group Π [septic shock without AF]. The incidence of new onset AF was (52%). Males & older people in our study developed new-onset AF more, Group I patients have comorbidity of cardiovascular diseases more, SIRS was manifested in group I more than group Π. Chest infection and Gram –ve organisms was more in group I. SOFA score & GCS medians was equal in both groups. AF occurrence was 57.7% in (2- <5 days), 16% in (5- <10 days) & 11.5% in (≥ 10 days). The median dose of N.A at onset AF was 1.0 mcg/kg/min. Treatment of acute AF was DC.Shock in 10 cases & amiodarone in 16 cases, after treatment 22 cases of 26 cases of AF regain NSR & 4 cases continue as AF, There was AF recurrence in patients who regained NSR in 9 cases. The median of days of stay in ICU was in group Π more than group I, The mortality was in group I statistically significant more than group Π, The median of max.dose of N.A reached in group I was statistically significant more than group Π, Duration of mechanical ventilation median was in group I more than group Π.
Conclusions: This prospective study found that new-onset AF is a very common complication in septic shock patients & most of it was occurred within < 5 days of septic shock onset. Older & male patients & patients with cardiovascular, metabolic, COPD, CVS comorbidity more developed AF. The most frequent site of infection associated with new onset AF was chest & the most frequent organism was Acinetobacter. Success rate of AF treatment was high & recurrence rate was about 60% in patients regain NSR. Mortality, need of N.A & need of M.V, were more in patients developed new onset AF.

KEY WORDS: Septic shock, Noradrenaline (N.A), Atrial fibrillation (AF), Antiarrhythmic drugs (amiodarone), cardioversion.

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INTRODUCTION

Septic shock, the most severe complication of sepsis, accounts for ~10% of all admissions to intensive care. Our understanding of its complex pathophysiology remains incomplete but clearly involves stimulation of the immune system with subsequent inflammation and microvascular dysfunction.(Hunter and Doddi, 2010) The cardiovascular system plays a key role in sepsis, and septic myocardial depression is a common finding associated with increased morbidity and mortality. Myocardial depression during sepsis is not clearly defined, but it can perhaps be best described as a global (systolic and diastolic) dysfunction of both the left and right sides of the heart. The pathogenesis of septic myocardial depression involves a complex mix of systemic (hemodynamic) factors and genetic, metabolic, and structural alterations. (Antonucci et al., 2014)

MATERIALS AND METHODS

This prospective study done on cases of septic shock admitted consecutively to critical care units in the main Alexandria university hospital during a 6 month period from 1st October 2013 till the end of March 2014, Inclusion criteria were Patients fulfilling the criteria of septic shock. Exclusion criteria Patients less than 18 years, Patients with chronic AF, Patients with known intermittent AF or episodes of AF in their history and Patients on antiarrhythmic drugs. There were 50 cases, they divided into two groups: Group I [septic shock with AF (26 cases)] & Group II [septic shock without AF (24 cases)].

Every patient enrolled in this study was subjected to: Demographic data: age & sex. Full history was taken, Thorough clinical examination was done for every patient. Assessment of level of conscious by using GCS or modified GCS on admission (Cook and Palma, 1989; Wijdicks et al., 2011), Assessment of severity of illness by calculating SOFA scores on admission (Jones et al., 2009), Lung injury score was done every day (Maskara et al., 2000). Laboratory investigations was done every day: CBC (HGB / HCT / RBCs / WBCs / Platelet count)(Williams et al., 1995), Hepatic function (serum albumin, prothrombin time, serum biliruben & liver enzymes AST& ALT),(Ellis et al., 1978; Tripodi et al., 2007) Renal function (serum creatinine & urea) and Arterial blood gases. ECG was done daily, Culture according to site of infection.

The outcome include: Duration of stay (days in ICU & in hospital), Need for vasopressors & inotrops (duration & dosage), Need for mechanical ventilation (duration in days) and Mortality.

Statistical analysis of the data (Kotz et al., 2006) **:** Data were fed to the computer and analyzed using IBM SPSS software package version 20.0 (Kirkpatrick and Feeney, 2013). Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. Significance of

the obtained results was judged at the 5% level. The used tests were: 1) Chi-square test: for categorical variables, to compare between different groups. 2) Fisher's Exact or Monte Carlo correction: correction for chi-square when more than 20% of the cells have expected count less than 5. 3) Student t-test: for normally quantitative variables, to compare between two studied groups. 4) Mann Whitney test: for abnormally quantitative variables, to compare between two studied groups. 5) Spearman coefficient: to correlate between two abnormally quantitative variables. 6) Kaplan-Meier Survival curve was used.

RESULTS

The incidence of AF in studied septic shock patients was (52%). Males in group I (69%) more than group Π (66.7%) & Females in group Π (33.3%) more than group I (30.8%), The median age in group I (69 years) statistically significant more than group Π (62 ys). Group I patients have past history (comorbidity) of cardiovascular diseases [HTN, CAD, HF&VHD], metabolic diseases [DM,CKD &Cancer] , COPD & CVS more than group Π, while in group Π past history of Alzheimer (1 case) & Bronchial asthma (1 case) & ICH (2 cases) which is (0) in group I, also Group Π has history of hepatic disease (4 cases) more than group I (1 case). Group I has history of cardiovascular drug use [BB ,CCB, ACEI &Digoxin], metabolic drugs [Insulin ,oral hypoglycemics & chemotherapy] & bronchodilators more than group Π , while Group Π patients have history of using corticosteroids & levodopa (1 case) each & sylimarine (2 cases) which is in group I (0 cases). Regarding SIRS in group I [leukocytosis, fever, tachypnea & tachycardia] found in cases more than group Π. As regarding indicators of inflammation: max.CRP & max.WBCs medians in group Π more than group I.

According to site of infection: chest (57%) & urinary tract (26%) in group I more than group Π (chest 54% & urinary tract 25%) , blood (8.3%) & wound (12.5%) in group Π more than group I (incidence of both is equal to 7.7%). The infecting organism: Culture negative in group Π (16.7%) more than group I (0%). Gram –ve (88.4%) in group I more than group Π (70.8%), [acinetobacter , klebsiella, citrobacter, E.coli] in group I more than group Π , while psudomonus is same in both groups. Grame +ve in group Π (12.5%) more than group I (11.5%), MRSA in group Π (3 cases) more than group I (2cases) & staphylococci in group I (1case) more than group Π (0).

Regarding median of mean investigations: HB. In group Π more than group I, platelets in group I more than group Π, Albumin in group Π more than group I, PT. in group I statistically significant more than group Π, Bilirubin in group I more than group Π, SGOT & SGPT in group Π more than group I, Creatinine & Urea in group I more than group Π, Electrolytes Na & K levels in group I more than group Π. Normal ABGs : equal in both groups (9) , Acidotic ABGs : in group I (13) more than group Π (10) , both metabolic acidosis (7) & respiratory acidosis (6) in group I more than group Π , Alkalotic ABGs in group Π (5) more than group I (4) , metabolic alkalosis in group I (3) more than group Π (2) , although respiratory alkalosis in group Π (3) more than group I (1). Regarding scores of severity of illness: SOFA score & GCS medians was equal in both groups (9 &14), Lung injury Score median was in group I (3) more than group Π (2), MGCS median was in group Π (17) more than group I (15.5).

Table (1): Comparison between the two studied groups according to patients characteristic

	Group I (With AF) (n= 26)	Group II (Without AF) (n= 24)	p
Sex (m/f)	18/8	16/8	0.846
Age (years)	68.0 ± 7.19	58.42 ± 14.24	0.006*
Co-morbidity			
Cardio vascular disease	30	19	-
Metabolic disease	27	17	-
Chest disease	7	4	-
CNS disease	4	4	-
Drug history			
Cardio vascular drugs	28	23	-
Metabolic drugs	17	9	-
Chest drugs	3	2	-
CNS drugs	0	1	-
SIRS			
Leukocytosis	20 (76.9%)	14 (58.3%)	0.159
Fever	16 (61.5%)	14 (58.3%)	0.817
Tachypnea	16 (61.5%)	10 (41.7%)	0.160
Tachycardia	13 (50.0%)	9 (37.5%)	0.374
Max CRP	146.0 (65.0 – 344.0)	171.5 (89.0 – 220.0)	0.426
Site of infection			
Chest	15 (57.7%)	13 (54.2%)	
UTI (urinary tract infection)	7 (26.9%)	6 (25.0%)	0.966
Blood	2 (7.7%)	2 (8.3%)	
Wound	2 (7.7%)	3 (12.5%)	
Infecting organism			
Culture Negative	0 (0.0%)	4 (16.7%)	0.046*
Gram –ve			
Acinetobacter	7 (26.9%)	4 (16.7%)	
Psoudomonus	5 (19.2%)	5 (20.8%)	
Klebsiella	6 (23.1%)	5 (20.8%)	0.982
Citrobacter	1 (3.8%)	0 (0.0%)	
E.coli	4 (15.4%)	3 (12.5%)	
Gram +ve			
MRSA	2 (7.7%)	3 (12.5%)	1.000
Staphylocoli	1 (3.8%)	0 (0.0%)	

Qualitative data were described using number and percent and was compared using Chi square test, while normally quantitative data was expressed in mean ± SD and was compared using student t-test, abnormally distributed data was expressed in median (Min. - Max.) and was compared using Mann Whitney test *: Statistically significant at $p \leq 0.05$

Table (2): Comparison between the two studied groups according to scores of severity of illness

	Group I (With AF) (n= 26)	Group II (Without AF) (n= 24)	p
SOFA	9.0 (7.0 – 18.0)	9.0 (5.0 – 16.0)	0.806
LIS	3.0 (1.0 – 8.0)	2.0 (1.0 – 8.0)	0.062
GCS	13.19 ± 2.0	12.67 ± 2.91	0.458
MGCS	14.92 ± 2.35	15.33 ± 3.57	0.631

Qualitative data were described using number and percent and was compared using Chi square test

Regarding characteristics of newly discovered AF in septic shock patients: AF occurrence was 57.7% in (2- <5 days), 16% in (5- <10 days) & 11.5% in (≥ 10 days). The median dose of N.A at onset AF was 1.0 mcg/kg/min. Treatment of acute AF was DC. Shock in 10 cases & cordarone (amiodarone) in 16 cases, after treatment 22 cases of 26 cases

of AF regain NSR & 4 cases continue as AF despite 2nd line treatment with DC.shock for patients received cordarone & cordarone for patients received DC.shock, There was AF recurrence in patients who regained NSR in 9 cases.

Table (3): Characteristic of AF according to onset, treatment and recurrence (n = 26)

	No. (%)
AF occurrence date (day)	
2 - <5	15 (57.7%)
5 - <10	8 (16.0%)
≥10	3 (11.5%)
Dose of NA at AF onset	0.93 ± 0.38
Rx (treatment)	
DC shock	10 (38.5%)
Cordarome (amudarome)	16 (61.5%)
Regain Normal sinus rhythem	
No	4 (15.4%)
Yes	22 (84.6%)
AF recurrence	
No	13 (59.1%)
Yes	9 (40.9%)

Qualitative data were described using number and percent, while normally quantitative data was expressed in mean ± SD.

The outcome of studied cases includes : ICU stay: The median of days of stay in ICU was in group Π (11 days) more than group I (10), although in group I (46.2%) of cases stay [4- <10 days] which is more than in group Π (41.7%) & in group I (53.8%) stay [10- <16 days] which is more than in group Π (50%), while in group Π [stay ≥ 16 days] was (8.3%) which is in group I was (0%). The mortality was in group I (53.8%) which is statistically significant more than group Π (25%).The median of days patients need N.A was in group Π (7.5 days) more than group I (5 days). The median of max. dose of N.A reached in group I was (1.1 mcg/kg/min) which is statistically significant more than group Π (0.8 mcg/ kg/min). Duration of mechanical ventilation median was in group I (7 days) more than group Π (6 days).

Table (4): Comparison between the two studied groups according to outcome

	Group I (With AF) (n= 26)	Group II (Without AF) (n= 24)	p
ICU stay (days)	9.96 ± 3.67	11.08 ± 2.83	0.235
Mortality			
No	12 (46.2%)	18 (75.0%)	0.038*
Yes	14 (53.8%)	6 (25.0%)	
Need NE (days)	50 (2.0 – 14.0)	7.50 (4.0 – 16.0)	0.225
Max. dose of Norepinephrine	1.10 (0.20 – 2.0)	0.80 (0.04 – 1.30)	0.003*
Need MV (days)	7.0 (3.0 – 14.0)	6.0 (4.0 – 16.0)	0.809

Qualitative data were described using number and percent and was compared using Chi square test, while normally quantitative data was expressed in mean ± SD and was compared using student t-test, abnormally distributed data was expressed in median (Min. - Max.) and was compared using Mann Whitney test.
*: Statistically significant at p ≤ 0.05

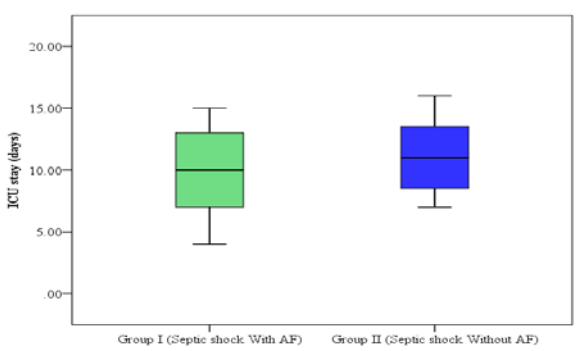

Figure (1): Comparison between the two studied groups according to ICU stay (days).

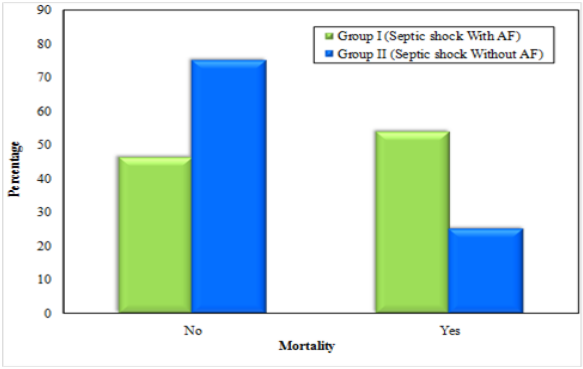

Figure (2): Comparison between two groups according to mortality.

In this prospective study the correlation in group I, There was a direct correlation between AF occurrence date & days of ICU stay & days of need of M.V., There was an inverse correlation between AF occurrence date & max. dose of N.A., There was a direct correlation between days of ICU stay & days of need of M.V, and There was an inverse correlation between days of ICU stay & max. dose of N.A. In group II, There was a direct correlation between days of ICU stay & days of need of M.V. In this prospective study the relation was: In group I: There was a relation between mortality & days of ICU stay & max dose of N.A. In group II: There was a relation between need of M.V. & days of ICU stay.

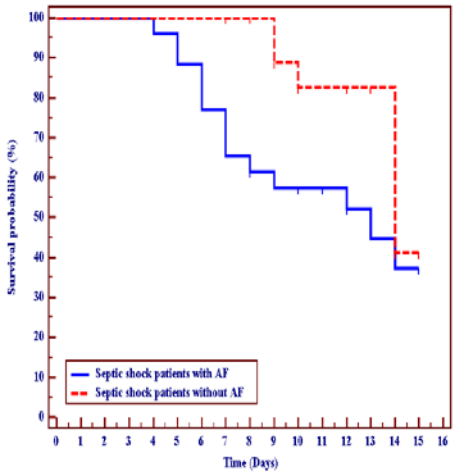

Figure (3): Kaplan-Meier survival curve for septic shock patients with new onset AF and septic shock with maintained NSR.

DISCUSION

New-onset AF when compared with finding of Meierhenrich *et al.* of 46%,(Meierhenrich et al., 2010) is slightly higher, Males & older people in this study developed new-onset AF more which is concordant with Meierhenrich *et al.* study & Walkey *et al.* (Walkey et al., 2011; Meierhenrich et al., 2010) Cardiovascular Comorbidities were associated with new-onset AF in this study, which is concordant with previous studies.

(Knotzer et a., 2000; Meierhenrich et al., 2010; Seguin et al., 2004). In this study SIRS found more in cases that developed AF which is concordant with Kindem *et al*.(Kindem et al., 2008), the most frequent organism was Acinetobacter while in Kindem *et al.* E. coli bacteremia was the most frequent. (Kindem et al., 2008) In this study SOFA score median was equal in both groups which is discordant with Meierhenrich *et al*. (Meierhenrich et al., 2010) AF occurrence & the dose of N.A at onset AF median was in agreement with previous studies. (Knotzer et a., 2000; Meierhenrich et al., 2010; Seguin et al., 2004) Treatment was possible in 84.6% of the patients which is nearly equal to results of Meierhenrich *et al*. (Meierhenrich et al., 2010) The mortality was statistically significant higher in patients who developed AF in this study, In agreement with previous studies.(Walkey et al., 2011; Meierhenrich et al., 2010)

CONCLUSION

This prospective study found that new-onset AF is a very common complication in septic shock patients & most of it was occurred within < 5 days of septic shock onset. Older & male patients & patients with cardiovascular, metabolic, COPD, CVS comorbidity more developed AF. The most frequent site of infection associated with new onset AF was chest & the most frequent organism was Acinetobacter. Success rate of AF treatment was high & recurrence rate was about 60% in patients regain NSR. Mortality, need of N.A & need of M.V, were more in patients developed new onset AF.

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