The Relationship between C - reactive protein and Outcome inCritically Ill Elderly

MotassemS.Amer, Sarah A. Hamza,Amira H. Mahmoud and Sarah H. Abou-Ziyan.

Department of Geriatrics and Gerontology Faculty of Medicine Ain Shams University, Cairo – Egypt
hasarah_2000@yahoo.com

Abstract: Background: Increasing the number of elderly patients admitted to intensive care units (ICU) increases the importance of having methods and markers to study the expected outcome. C- reactive protein (CRP) can be an important method related to the outcome of those patients. **Objectives**:To find out the relation between the levels of serum CRP concentrations and the outcome of critically ill elderly admitted to ICU.**Method**:A prospective study was performed in Geriatric ICU in Ain Shams University Hospitals among 100 critically ill elderly patients admitted for 48 hours or more.Each patients was subjected to comprehensive geriatric assessment, measurement of CRP initially and after 48 hours,Acute Physiological and Chronic Health EvaluationII Score (APACHE II) daily assessment of morbidity using Sequential Organ Failure Assessment Score (SOFA).**Results**:49 patients died with no significant relation with neither age nor gender regarding mortality (P>0.05). The first cause of mortality was among patients admitted due to cerebrovascular stroke. Those who need mechanical ventilation significantly had more mortalities (P= 0.001). The mean CRP among the dead participants on admission and after 48 hours were 106.2±62 mg/L, 105.7±65mg/L respectively while among the survivors were 73.5±55mg/L, 54±3mg/L respectively and the difference was significant. Mean and maximum SOFA score, APATCHE, risk of mortality were significantly higher in cases of mortality (P< 0.01). Correlating them with CRP revealed significant positive correlation with SOFA mean, APACHE expected mortality and duration of ICU stay (P= 0.03,0.009, 0.01& 0.02) respectively.**Conclusion:** CRP is an important and sensitive marker in critical illness. It can reflect and predict prognosis. It is correlated with commonly used scales for evaluating critically ill elderly.

[Motassem S. Amer, Sarah A. Hamza, Amira H. Mahmoud, and Sarah H. Abou-Ziyan. **The Relationship between C - reactive protein and Outcome inCritically Ill Elderly**. *Life Sci J* 2013; 10(3): 2261-2265]. (ISSN: 1097-8135). http://www.lifesciencesite.com. 333

Key words: elderly, intensive care, C- reactive protein.

1. Introduction:

Aging brings an increased predisposition to critical illness. The prevalence of critical illness has increased andmany more people are now surviving these conditions due to life-prolonging cures and operations that are becoming increasingly available [(1)].A substantial proportion of patients admitted to intensive care units (ICUs) are elderly patients. More than half (55.8%) of all ICU days are occupied by patients older than 65[(2)].

In ICU population, elevated concentrations of serumC-reactive protein(CRP) on ICU admission are correlated with an increased risk of organ failure and death [(3)].

Theprinciples of intensive care management are the assessment of severity of illness and stabilization of life threatening physiological abnormalities, besides preventing deterioration and improvement as the diagnosis is made and treatment of underlying definitive disease process is initiated[(4)].

The role of CRP and its association witheither complications andoutcome had been studied in some research work[(5-8)].

This study aimed at finding out the relation between the levels of serum C-reactive protein concentrations and the outcome of critically ill elderly admitted to the intensive care unit.

2. Method:

Aprospective study was performed among all patients admitted to ICU of the Geriatrics and Gerontology Department – Ain shams university hospitals. It is considered the only ICU for critically ill elderly in Egypt.The follow-up period was done during the duration of ICU stay ended with either discharge or mortality.100 elderly patients admitted duringthe period from (June 2012 to December 2012). All patients were 60 years and over.

They were admitted to the ICU more than 48hours on the other hand patients admitted to the ICU less than 48 hours were excluded.All participants underwent; comprehensive geriatric assessment, assessment of severity of illness at admission using Acute Physiological and Chronic Health Evaluation Score (APACHE II)[(9)]anddaily assessment of morbidity using Sequential Organ Failure Assessment Score (SOFA)[(10)].

Meanwhile Laboratory assessments ofcomplete blood count (CBC), serumsodium(Na), Potassium (K), liverenzymes (aspartateaminotransferase (AST) & alanine

aminotransferase (ALT)), blood urea nitrogen(BUN), serumcreatenin and CRP measured at day 0 (within 24 hours of admission) and day 2 (after 48 hours of admission).CRP was measured at day 0 (within 24 hours of admission) and day 2 (after 48 hours of admission).

Laboratory measures were all performed in Ain Shams University Central Laboratories.

Assessments of outcome of ICU stay, in the form of mortality or discharge.

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science. Data was presented and suitable analysis was done according to the type of data obtained for each parameter.Descriptive statistics in the form of mean, Standard deviation (±SD), Median, Minimum and maximum values (range) for numerical data and frequency and percentage of non-numerical data were performed. Analytical statistics; student T, correlation analysis (using Pearson's method) and Chi-Square test were used. $P< 0.05$: is considered "Significant (S)".

3. Results:

The study included 100 participants 29 males and 71 females, all of them are ≥ 60 years old with mean age 68± 8.1 years (range 60-94 years).The causes of admission are presented in table (1)and the distribution of comorbidities is present in table (2).

After the period of follow up 49patientsdied 14 males (28.6%) and 35 females (71.4%) with no significant difference between genders regarding mortality with mean age 67.9±8 years compared to 68.8±8 years for living participants with also no significant difference.

Revising the cause of admissionof the dead participants revealed that 44.9% admitted by cerebrovascular stroke and 22.4% were shocked followed by 10.2% admitted due to acute coronary syndrome, 8.2 % had respiratory failure and the rest due to other meciliniaus causes.

Studying the relation between the cause of admission and mortality regarding that stroke, shock, acute coronary syndrome, respiratory failure and hepatic encephalopathy revealed no significant relations P= 0.8,0.2, 0.1, 0.3 &0.2 respectively.But those who need mechanical ventilation significantly had more mortalities (P= 0.001).

Studying the probabilities of mortality by CRP on admission is 65% while after 48 hours it was 67.7% (Figures 1a&b).

The mean CRP among the dead participants on admission and after 48 hours were 106.2±62 mg/L, 105.7±65mg/L respectively while among the survivors73.5±55mg/L, 54±3mg/L respectively and the difference was significant both on admission and after 48 hours.

Similarly the difference between dead participants and survivorsregarding other laboratory measures were presented in table (3).

Lower mean platelets among dead patients compared to living patients and the difference is significant statistically. Also higher renal functions were significantly related tomortality.

Comparing mean and maximum SOFA score, APATCHE, risk of mortality and duration of ICU revealed that the first four variables were significantly higher in mortality (Table 4). Meanwhile correlating them with CRP revealed significant positive correlation with SOFA mean, APACHE expected mortality and duration of ICU stay(r=0.21,0.26,0.25&0.22 respectively and p= 0.03,0.009, 0.01& 0.02 respectively.

Table (1) Distribution of causes of admission to ICU among studied patients(N=100)

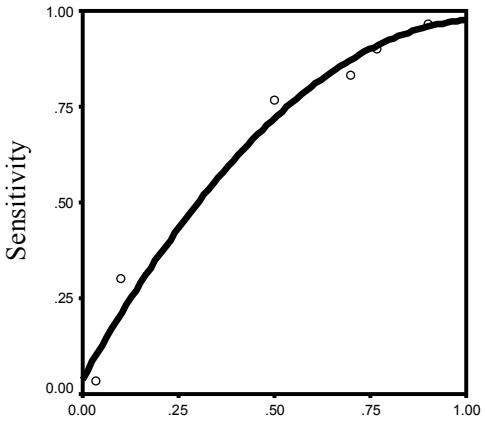
Cause of admission	%
Stroke	**44.0**
Shock	**18.0**
Acute coronary syndrome	**16.0**
Respiratory failure	11.0
Post arrest	6.0
Hepatic encephalopathy	4.0
Others	13.0
Pervious admission to ICU	10.0

ICU: Intensive care units

Table (2) Distribution of history of chronic diseases among studied subjects

Chronic disease	%
Diabetes mellitus	**54.0**
Hypertension	**65.0**
Heart failure	**42.0**
Stroke	30.0
COPD	19.0
Liver disease	24.0
Renal disease	19.0
Cancer	13.0
Gastric disease	15.0
Others	9.0
Previous admission to ICU	10.0

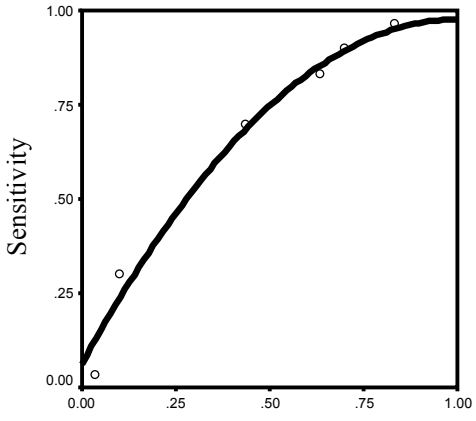
COPD chronic obstructive pulmonary disease



Area under the curve 0.650 95% CI (0.54-0.758)

Figure(1a)ROC curve for detection of mortality by CRP on admission:

The probability of detection of mortality by CRP on admission is 65% using the ROC curve



Area under the curve 0.677 95% CI (0.573-0.782)

Figure (1b) ROC curve for detection of mortality by CRP after 48 hours

The probability of detection of mortality by CRP after 48 hours of admission is 67.7% using the ROC curve

Table (3) Relation between mortality and the mean laboratory parameters

Variables	Living N=51		Dead N=49		T	*P*
	Mean	SD	Mean	SD		
Total leucocytic count (1000/uL)	13.4	±5.8	14.1	±6.5	0.5	0.6
Hemoglobin (g/dl)	11.1	±2.5	10.4	±2.8	1.2	0.2
Hematocrit (%)	36.1	±7.2	34.8	±7.8	0.8	0.4
Platelets (1000/uL)	252.8	± 120.1	**196.6**	±94.8	2.5	**0.01***
AST (IU/L)	30.2	±23.0	36.0	±35.7	0.9	0.3
ALT (IU/L)	27.3	±22.8	40.2	±64.8	1.3	0.1
Albumin (g/dl)	2.9	±0.6	2.7	±0.7	1.5	0.1
BUN (mg/dl)	37.9	±33.9	**55.9**	±42.0	2.3	**0.02***
Creatinine (mg/dl)	1.9	±2.8	**3.2**	±3.5	2.1	**0.04***
Serum Na (mmol/L)	134.6	±9.6	133.4	±9.7	0.5	0.5
Serum K (mmol/L)	4.1	±0.9	4.1	±1.0	0.1	0.8

AST aspartate aminotransferase ALT alanine aminotransferase BUN Blood urea nitrogen Na SodiumK Potassium

Table (4) Relation between mortality and the mean SOFA and APACHE:

Variables	Living N=51		Dead N=49		T	*P*
	Mean	SD	Mean	SD		
SOFA mean	2.55	2.1	**8.2**	3.9	9.0	**<0.001***
SOFA maximum	3.3	2.5	**10.2**	4.0	10.3	**<0.001***
APACHE	17.0	6.2	**24.3**	6.1	5.8	**<0.001***
Mortality risk %	28.1	16.3	**46.3**	17.8	5.2	**<0.001***
Duration of stay in ICU	4.3	2.3	**5.5**	3.8	1.8	0.07

SOFASequential Organ Failure Assessment Score
APACHEAcute Physiological and Chronic Health Evaluation

4. Discussion:

In the current study we aimed at studying the relation between CRP level and outcome of critically illelderly admitted to Geriatric ICU and the different variable affecting those parameters.

Among the hundred admitted subjects, forty-nine (49%) patients died and the rest survived to ICU discharge.There was no statistically significant difference between dead and surviving subjects as regards their age. Both **Blancas*et al.*** [(11)]**and Vosyliuset *al.*** [(12)]discussedthe same issue and their results were supporting the concept that mortality is significantly more among older agegroups. Similarly in the current study there was no significant difference between males and females regarding mortality. Literatures discussing this issue before reported that females had different pattern [(13)]**.** Few years later **Mardini*et al.*** [(14)]reported that whether the high mortality observed in females is due to inherent physiologic differences between sexes or if treatments varied between sexes requires further studyare needed and we support this in the current study.

In our study we examined the distribution of the causes of admission to the ICU among studied subjects and their relation to mortality. This can be compared to Centers of disease control (CDC) who reported that heart disease followed by cancer than chronic lower respiratory disease followed by stroke are the first four leading causes of death in the United states. But **Mayr*et al.*** [(15)] found that central nervous system failure and cardiovascular failure were the two most important risk factors for death in the ICU.

What should be a serious point is that our study showed that mechanical ventilation was related to increased ICU mortality in a highly significant pattern, 92.9% of mechanically ventilated patients died, this was supported by previous studies [(16, 17)]**.**

The probability of detection of mortality by CRP on admission was 65% using the ROC curve. The probability of detection of mortality by CRP after 48 hours of admission was 67.7%, showing that CRP after 48 hours of admission has a higher probability for detection of mortality.

We found a higher mean CRP at entry to ICU among dead subjects compared to surviving subjects. Besides, there was a higher mean CRP after two days among dead subjects compared to surviving subjects this agreed with different previous studies. Lobo ***et al.*** [(18)] Schmit and Vincent [(19)]discussed the relation between CRP and outcome in different ways.

Mean platelets count was lower among dead patients compared to surviving patients. Similarly mean BUN and creatinine were higher among dead subjects compared to surviving subjects and the difference was statistically significant. This spot light on the importance of considering those variables especially that elderly patients usually suffer multiple chronic comorbidities.

Studying the relation between mortality, APACHE II and SOFA scores showed higher mean APACHE score among the dead patients compared with the surviving patients and the difference was highly significant statistically. Similarly was the relation regarding SOFA scores and mean mortality risk.

Correlation between CRP and SOFA score, APACHE, expected mortality and duration of stay in ICU showed a highly significant positive correlation between CRP at entry to ICU and CRP after 48 hours. Meanwhile a positive correlation between CRP and mean SOFA score were detected and a positive correlation between CRP and APACHE, expected mortality and the duration of stay in ICU.

This agreed with **Lobo *et al.*** [(18)]**Van le *et al.*** [(20)]**.Mayr*et al.*** [(15)] found that ICU survivors had a significantly shorter ICU stay than did non-survivors. ICU non-survivors did not die early in the course of the disease but primarily in the period of prolonged critical illness. This finding underlines the emerging phenomenon of chronic critical illness.

Although the current study is a single-center study, and the analysis of factors associated with survival after ICU discharge were not included such as repeated ICU admissions or institutionalization, we can say that CRP can be considered an important parameter in evaluation and prediction of patients outcome, but further studies are required to evaluate health related quality of life in patients in the years following ICU discharge. Similar studies among surgical ICU patients can be also considered interesting research points. Thus we can recommend that CRP level should be measured in critically ill elderly; however it should always be interpreted in the clinical context. CRP levels alone can never be diagnostic, but should be used to support other clinical signs and symptoms. APACHE II and SOFA score should be included in assessment of critically ill since they help to categorize mortality risk and prognosis of patients during the period of ICU stay.

Conclusion:

CRP is an important and sensitive marker in critical illness. It can reflect and predict prognosis. It is correlated with commonly used scales for evaluating critically ill elderly.

Acknowledgments:

The authors acknowledge to the central laboratories in Ain shams university hospitals.

References:

1-Milbrandt EB, Eldadah B, Nayfield S, *et al.* Toward an Integrated Research Agenda for Critical Illness in Aging. Am J RespirCrit Care Med 2010; 182(8): 995-1003

2-Hofhuis JG, Spronk PE, van Stel HF *et al.*.Quality of life before intensive care unit admission is a predictor of survival. Critical Care.2007; 11 (4): 78.

3-Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest. 2003; 111 (12): 1805–12.

4-Tritchard RF, Grant IS. Critical illness, In Boon NA, Colledge NR , Walker PR *et al.*eds, Davidson's principles & practice of medicine, 21st edition, 2010.Pp 177-201.

5-Cox ML, Rudd AG, Gallimore R, *et al.*Real-time measurement of serum C-reactive protein in the management of infection in the elderly. Age Ageing.1986; 15 (5): 257-66.

6- Lobo SM, Lobo FR, Bota DP, *et al.*C-reactive protein levels correlate with mortality and organ failure in critically ill patients". Chest.2003; 123 (6): 2043–9.

7-Presterl E, Staudinger T, Pettermann M, *et al.*Cytokine profile and correlation to the APACHE III and MPM II scores in patients with sepsis. Am J RespirCrit Care Med. 1997; 156 (3): 825-32.

8- Wieland A, Kerbl R, BergholdA,*et al.*.C-reactive protein (CRP) as tumor marker in pediatric and adolescent patients with Hodgkin disease; Med Pediatr Oncol. 2003; 21–25:5.

9-Knaus WA, Draper EA, Wagner DP*et al.* "APACHE II: a severity of disease classification system". Critical Care Medicine.1985; 13 (10): 818–29.

10-Jones AE, Trzeciak S, Kline JA. The Sequential Organ Failure Assessment scores for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. Crit Care Med. 2009; 37 (5): 1649-54.

11-Blancas R, Martinez-Gonzalez O, Vigil D, *et al.*Influence of age and intensity of treatment on intra-ICU mortality of patients older than 65 years admitted to the intensive care unit. European Geriatric Medicine. 2012; 3 (5): 290–4.

12- Vosylius S, Sipylaite J, Ivaskevicius J. Determinants of outcome in elderly patients admitted to the intensive care unit; Age Ageing. 2005;34(2): 157-62.

13-Fowler RA, Sabur N, Li P,*et al.*Sex and age based differences in the delivery and outcomes of critical care. CMAJ.2007; 177 (12): 1513-9.

14- Mardini L, Lipes J, and JayaramanD .Increased female mortality after ICU admission and its potential causes.CCCF oral presentations available at http://www.criticalcarecanada.com/presentations/2012/.

15-Mayr VD, Dünser MW, Greil V, *et al.*Causes of death and determinants of outcome in critically ill patients,Critical Care.2006; 10 (6): 154.

16-Sudarsanam TD, Jeyaseelan L, Thomas K, *et al.*Predictors of mortality in mechanically ventilated patients. Postgrad Med J. 2005; 81 (962): 780-3.

17-Gajic O, Afessa B, Thompson BT, *et al.*Prediction of death and prolonged mechanical ventilation in acute lung injury.Critical Care. 2007; 11 (3): 53.

18-Lobo SM, Lobo FR, Bota DP, *et al.*C-reactive protein levels correlate with mortality and organ failure in critically ill patients". Chest.2003; 123 (6): 2043–9.

19-Schmit X, Vincent JL.The time course of blood C-reactive protein concentrations in relation to the response to initial antimicrobial therapy in patients with sepsis.*Infection.2008*;**36 (3):** 213-9.

20- Van Le L, Fakhry S, Walton LA, *et al.*.Use of the APACHE II scoring system to determine mortality of gynecologic oncology patients in the intensive care unit; Obstet Gynecol. 1995, 85:53–6.

9/12/2013