Relation between C-reactive protein level and one year mortality among elderly patients with heart failure.

Nora Abdel-Khalek Abdel-Salam*,WalaaWessamAly*,Sarah Ahmed Hamza*,Ahmed Kamel Mortagy*,Hossam Mosfata Fahmy**

* Geriatrics and Gerontology Department.

**Clinical Pathology Department.

Faculty of Medicine - Ain Shams University

Abstract:

Background: Data suggests that inflammatory processes may play a role in the development of heart failure and death after myocardial infarction independently of other conventional prognostic indicators. C- reactive protein (CRP) was found to be associated with increased risk of heart failure and death, independently of age, sex, myocardial infarction severity, co morbidity, previous myocardial infarction and recurrent ischemic events. Objectives: To assess the relation between CRP level and one year mortality among elderly patients with heart failure. Methods: Serum CRP level was measured in 100 elderly patients with heart failure diagnosed by Criteria of New York Heart Association (NYHA). Patients were followed by telephone for one year to assess relation between CRP level and one year mortality among elderly patients with heart failure. Results: Higher mortality percentage was found among patients with high level of CRP with the mean CRP being higher among patients who died compared with living patients, but with no significant difference (P-value>0.05).The highest mean levels of CRP were found among patients with left ventricular systolic and diastolic failure, although no statistical significant relation could be detected (P-value>0.05). No significant relation was found between each of age and Ejection Fraction (EF)and CRP. Conclusion: Patients who had high level of CRP had greater risk of mortality. Further studies with larger number of patients and longer period of follow up are recommended. Still measuring CRP for patients with HF can be of great values and anti-inflammatory can be beneficial unless contraindicated. Key words: CRP, mortality, elderly patients, heart failure.

Introduction

Congestive heart failure is the leading cause of admissions to hospitals among the elderly people with hospital admissions being a significant portion of the total costs. (1)Elderly patients with heart failure still have a three-fold higher mortality compared with age matched patients without heart failure.(2)

The prognosis following a new diagnosis of heart failure in the general population is poor. The risk of mortality is particularly high in the early period after diagnosis with approximately 25-30% not surviving six months. (3) In developing countries heart failure is the most common diagnosis with a high mortality. (4) CRP plays an active role in endothelial dysfunction and atherosclerotic plaque formation and progression and has been found within atherosclerotic plaques. Indeed, CRP down-regulates endothelial nitric oxide synthase (eNOS) transcription in endothelial cells (EC) and destabilizes eNOS mRNA, resulting in decreased nitric oxide (NO) release (5). This inhibition of NO production facilitates endothelial cell apoptosis and blocks angiogenesis (5). It also up-regulates angiotensin type-1 receptor (AT-1) in vascular smooth muscle cells and stimulates migration, proliferation, neointimal formation, and reactive oxygen species (ROS) production(6).

Higher CRP levels were observed in patients with higher NYHA functional class and were related to higher rates of readmission and mortality (7). The current study aimed at assessing the relationship between CRP and one year mortality among elderly patients with heart failure Patients and methods A prospective study was performed among 130 elderly patients with decompensated heart failure (class III, IV) diagnosed by Criteria of New York Heart Association (NYHA), recruited from the different medical wards in Ain Shams University Hospital during a 12 months period from August 2011 to August 2012. Cases with acute inflammatory states were not included in the study. Each patient was subjected to: - Complete examination including general examination with special consideration to cardiological examination.

CRP measurement: Blood samples were collected on the first day of

admission into vacuum tubes at bedside (peripheral vein), fresh serum was collected by centrifuging clotted blood. All samples were then frozen to –20 C and were stored at that temperature until analysis. The CRP reagent kit is based on the principle of the latex agglutination assay and performed in central lab of Ain shams University Hospital. - Echo cardiography - Patients were followed by telephone

every 3 months for one year to assess relation between CRP level and one year mortality among elderly patients with heart failure, there were 30 dropped cases so the final analysis was done on 100 patients, the causes of death in all died patient were complications of heart failure Results: The data analysis was performed on 100 elderly patients, 46 males representing 46% and 54 females representing 54%.

The age of participants ranged from 62 - 88 years old with mean 66.28±8.9 years. High mortality percentage among patients with high level of CRP was recorded but there was no statistically significant difference (P-value >0.05) Table (1) Mean CRP was higher among patients who died compared with living patients, although no significant difference. (P-value >0.05) Table (2) Highest mean levels of CRP were found among patients with left ventricular systolic and diastolic failure, although no statistically significant relation could be detected (P-value>0.05)Table (3)

There was no significant correlation between age and CRP($r = -0.046$, $p = 0.647$) , and no significant correlation between Ejection Fraction (EF) and CRP ($r = -0.179$, $p = 0.075$) .

Table (1): Relation between CRP and mortality

Table (2) Relation between mortality and the level of CRP

Table (3) Comparison between mean levels of CRP and different types of heart failure

Discussion:

Predicting mortality among elderly patients with serious medical conditions had been considered an important recent research issue. This had its impact in the development of the plan of management in Geriatric practice.

The current study shows a high mortality percentage among patients with high CRP, but there was no statistically significant found. This may be explained as one -year follow-up period may not be long enough to demonstrate the effects of inflammation on risk of death in patients with heart failure and it is possible that in participants, the effect of CRP may be obscured by the presence of other co morbidities not related to inflammation. It is worth mentioning that excluding patients with other cause that may elevate the CRP level could not be applied because the majority of elderly patients are having multiple conditions but cases

with evident inflammatory problems were excluded. This can be compared to Störk et al.,2006 who reported through a prospective study in 403 independently living elderly men that increasing tertiles of CRP, were independently associated with all-cause of cardiovascular mortality occurring during 4 years of follow-up.(8) The markedly increases in CRP during an inflammatory response; predict the development of coronary heart disease and cardiac failure. Additionally, CRP may directly promote the development of atherosclerosis, through complement activation, tissue damage and activation of endothelial cells (9).The findings that CRP predicts morbidity and mortality in patients with established Heart failure and progression of Heart failure in patients after myocardial infarction (10) and higher CRP levels being associated with poorer NYHA functional class and greater severity of HF(11) , support the current results.

Ridker and his colleagues, (2000) in a cohort of apparently healthy women, showed that baseline CRP level was a strong predictor of the incidence of cardiovascular events during a3-year follow-up period (12). Kuller et al., (1996) also demonstrated a strong association between CRP and the risk of CHD death (13). However, Harris et al., (1999) did not agree with that and reported that in older persons, the relation between IL-6, CRP, and the risk of mortality was similar for those with and without CVD (14). In the current study the highest mean levels of CRP were found among patients with LV systolic and diastolic failure, although no statistically significant relation could be detected. These results can be explained by considering the narrow range between the CRP levels in the patients with different types in addition to some cardiodepressive mechanisms of cytokines that may also play a role in the diastolic phase. Similarly, Karpiński et al., (2008) studied the relationship between CRP and left ventricular function in patients with MI, and found a significant correlations between increased CRP level and impaired LV systolic and diastolic function indicating the possible involvement of this factor in post infarction cardiac damage, and it was an independent predictor of LV systolic and diastolic dysfunction 6 months after MI (15).

Although there is increased inflammatory activity in elderly populations (inflamm-ageing) resulting from a global reduction in the capacity to cope with a variety of stressors (16), there was no significant correlation between age and CRP in the current study Conclusion: The study revealed that patients who had high level of CRP had greater risk of mortality. And the highest mean levels of CRP were found among patients with left ventricular systolic and diastolic failure. Further studies

with larger number of patients and longer period of follow up are recommended. Still measuring CRP for patients with HF can be of great values and anti-inflammatory can be beneficial unless contraindicated.

References:

1. Balady, GJ, Williams, MA, Ades, PA, et al. Core components of cardiac rehabilitation/secondary prevention programs. Circulation .2007; 115:2675
2. Rosamond W, Flegal K, Friday G, et al Heart disease and stroke statistics . Circulation. 2007; 115: 69–171.
3. Barretto AC, Del Carlo CH, Cardoso JN, et al. Hospital readmissions and death from heart failure .Arq Bras Cardiol .2008; 91: 335-41.
4. Siswanto BB, Munawar M, KusmanaD, et al. Predictors of Mortality and Rehospitalization of Acute Decompensated Heart Failure at Six Months Follow Up. Crit Care & Shock. 2006 ; 9: 61 – 67
5. Verma S, Li SH, Badiwala MV, et al. Endothelin antagonism and interleukin-6 inhibition attenuate the proatherogenic effects of Creactive protein. Circulation .2002; 105:1890-6.
6. Pasceri V, Willerson JT and Yeh ET. Direct proinflammatory effect of C-reactive protein on human endothelial cells. Circulation 2000; 102:2165-68.
7. Mart´ınez A J, Diez BL, Arencibia GL, et al. C-reactive protein as a predictor of improvement and readmission in heart Failure M. The European Journal of Heart Failure .2013;(4):331–36
8. StörkS,Richard A, Ewout W ,et al. Prediction of Mortality Risk in the Elderly. The American Journal of Medicine.2006 ; (119): 519-25.
9. Vasan RS, Sullivan LM, Roubenoff R et al. Inflammatory markers and risk of heart failure in elderly subjects without prior myocardial infarction:. Circulation .2003; 107: 1486–91.
10. Lamblin N., Mouquet F., Hennache B., et al. High-sensitivity C-reactive protein: potential adjunct for risk stratification in patients with stable congestive heart failure. Eur Heart J .2005; 26:2245-50.
11. Anand I.S., Latini R., Florea V.G., et al. C-reactive protein in heart failure: prognostic value and the effect of valsartan. Circulation .2005; 112:1428-34.
12. Ridker PM, Hennekens CH, Buring JE, et al. C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women. N Engl J Med.2000; 342:836–43.
13. Kuller LH, Tracy RP, Shaten J, et al. Relation of C-reactive protein and coronary heart disease in the MRFIT nested case-control study.Am J Epidemiol. 1996 ; 144:537–47.

14. Harris TB, Ferrucci L, Tracy RP, et al. Associations of elevated Interleukin-6 and C-reactive protein levels with mortality in the elderly. Am J Med. 1999; 106:506 –12.
15. Karpiński L, Płaksej R, Kosmala W, et al. (Serum levels of interleukin-6, interleukin-10 and C-reactive protein in relation to left
ventricular function in patients with myocardial infarction treated with primary angioplasty. KardiolPol .2008; 66: 1279-85.
16. Franceschi C, Bonafé M, Valensin S, et al. Inflamm-aging. An evolutionary perspective of immuno-senescence. Ann NY Acad Sci .2000; 908: 244-54.