High-sensitivity c-reactive protein (hs-CRP) value with 90 days mortality in patients with heart failure

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Abstract. Hospitalization in patients with chronic heart failure is associated with high rates of mortality and morbidity that during treatment and post-treatment. Despite the various therapies available today, mortality and re-hospitalization rates within 60 to 90 days post-hospitalization are still quite high. This period is known as the vulnerable phase. With the prognostic evaluation tools in patients with heart failure are expected to help identify high-risk individuals, then more rigorous monitoring and interventions can be undertaken. To determine whether hs-CRP have an impact on mortality within 90 days in hospitalized patients with heart failure, an observational cohort study was conducted in 39 patients with heart failure who were hospitalized due to worsening chronic heart failure. Patients were followed for up to 90 days after initial evaluation with the primary endpoint is death. Hs-CRP value >4.25 mg/L we found 70% was dead and hs-CRP value <4.25 mg/L only 6.9% was dead whereas the survival within 90 days. p:0.000. In conclusion, there were differences in hs-CRP values between in patients with heart failure who died and survival within 90 days.

1. Introduction
Heart failure is a complex clinical syndrome resulting from structural or functional damage from ventricular filling or blood pumping.[1,2] Heart failure is a progressive health problem with high mortality and morbidity in both developed and developing countries including Indonesia.[1-4]

In Indonesia, the age of Heart failure patients is relatively younger than in Europe and the US are accompanied by a more severe clinical appearance.[4] Based on data from the Ministry of Health in 2014, the prevalence of Heart failure disease in Indonesia in 2013 is 0.3% or approximately 530,068 people. The prevalence of heart failure shows an exponential pattern that increases with age and about 6 - 10% of individuals over 60 years.[4-7]

Several studies have suggested that congestive heart failure should be regarded as a neurohormonal model, where the heart failure progressiveness results from excessive expression of biologically active molecules that can express toxic substances to the heart and circulation. Since the discovery of inflammatory cytokine activation in patients with congestive heart failure, There is a trend of studies to develop knowledge about its contribution to the progressive congestive heart failure.[2,8]

2. Methods
This type of research is observational with prospective cohort study method.

Data collection, including name, age, sex, a medical record number, address, telephone number, anamneses, physical examination, investigation including laboratory examination. Imaging, and
echocardiography. Blood sampling for hs-CRP was performed. Researchers take all subjects who met the study criteria. The patients are followed up for 90 days from the initial examination. And then information about the patient's condition is obtained based on a direct encounter with the patient, or by communicating via telephone with the patient or family.

The normality test using Shapiro-Wilk test. To see the comparative in the mean of the variables between the survival and mortality group is used independent T-test if normal distribution and if otherwise the Mann-Whitney test is used. To see the different relationship between categorical variables is used chi-square test. The results p <0.05 were considered significant and used the SPSS v.20 program.

3. Results
This study was conducted in the inpatient ward of Haji Adam Malik hospital Medan starting November 2016 with the number of samples of 39 people who have met the inclusion criteria so that it can be included in the study. All subjects were then followed up for 90 days from the initial examination. The total of a number of study subjects were 39 peoples, 9 subjects died during the follow-up period of 90 days.

Table 1. Characteristics of the subjects.

|                          | Total (n = 34) | Mortality (n = 16) | Survival (n = 18) | P  |
|--------------------------|---------------|-------------------|------------------|----|
| Demographics             |               |                   |                  |    |
| Male                     | 27 (69.2)     | 6 (66.7)          | 21 (70)          | 0.849 |
| Female                   | 12 (30.8)     | 3 (33.3)          | 9 (30)           |     |
| Age, average, year       | 54.46 (13.82) | 64.11 (9.57)      | 51.56 (13.6)     | 0.015 |
| NYHA Classification      |               |                   |                  |    |
| Class III                | 31 (79.5)     | 5 (55.6)          | 26 (86.7)        | 0.043 |
| Class IV                 | 8 (20.5)      | 4 (44.4)          | 4 (13.3)         |     |
| Clinical and Laboratory Data. |         |                   |                  |    |
| Systolic blood pressure  | 130 (15.38)   | 135 (14.2)        | 128.3 (15.5)     | 0.184 |
| Diastolic blood pressure | 74.6 (9.41)   | 77.7 (10.9)       | 73.6 (8.89)      |     |
| Hs-CRP                   | 2.7 (2.00)    | 4.9 (1.68)        | 2.13 (1.62)      | 0.001 |
| Echocardiography         |               |                   |                  |    |
| Ejection fraction (EF), %| 49 (13.46)    | 37.88 (4.34)      | 52 (13)          | 0.001 |

The male subjects were dominant in both study groups, 21 (70%) in the survival group and 6 (66.7%) in the mortality group. Based on functional capacity, the majority of patients enter the group with the functional capacity of NYHA III. Mean age was significantly different in the subjects who mortality compared to the survival subjects (p <0.05). In the clinical data, there was no difference in mean systolic blood pressure and diastolic blood pressure in both study groups.

With Mann-Whitney test obtained p-value<0.05 it can be concluded that there was a significant difference between hs-CRP at the mortality group and survival group (Table 1). From the results of echocardiography examination found the significant difference of ejection fraction between mortality and survival groups.

The boxplot graph of the difference in hs-CRP value for survival and mortality groups within 90 days. It can be seen that median hs-CRP values in the group of subjects who mortality was higher than the survival groups. The statistically significant differences were found between these two groups (p = 0.001).
Figure 1. The boxplot graph of the difference in hs-CRP values for survival and mortality groups within 90 days.

The differences hs-CRP value with 90-Day Mortality in Patients with Heart Failure by using chi square test, hs-CRP value >4.25 mg/L we found 70% and hs-CRP value <4.25 mg/L that found 6.9% in mortality subjects, whereas the hs-CRP value >4.25 mg/L that found 30% and hs-CRP value <4.25 mg/L we found 93.1% in survival subjects within 90 days, so there were the differences hs-CRP value between mortality and survival subjects within 90-days in patients with heart failure (p = 0.000).

Table 2. The differences hs-CRP value with 90-days mortality in patients with heart failure.

| Hs-CRP (mg/L) | 90 days-mortality | Total | p     |
|--------------|-------------------|-------|-------|
| >4.25        | Yes: 7 (70)       | 10    | 0.000 |
| <4.25        | No: 3 (30)        | 29    |       |

4. Discussion

In this study with a total of 39 subjects, there was a significant mean age difference between the mortality (64.11±9.57) and the survival group (51.56±13.69), p<0.05. The mortality group in this study had characteristics of older age. This result is in accordance with a study by Gheorghidae who received subjects with an early mortality and rehospitalization had the characteristic with the older age of 68.2±13 years compared to the non-group of 65.2±12.0 in the live group (p<0.001).[9]

Age is the most important factor determining the condition of individual cardiovascular health. Aging is associated with a progressive decrease in a number of physiological processes, leading to an increased risk of illness as well as complications.[10] As a result of the aging process; there is an overall setback of anatomical and functional structures.

The frailty and comorbid disease are characteristic of this age group and contribute to unexpected events at care and post-care. A study by Gustaffson et al. found that an increase in age independently associated with short-term mortality as well as long-term patients in hospitalized heart failure patients. Each 10-year-old increase in patients with heart failure that aged <60 years have significantly increased the risk of death within 30 days (Relative Risk (RR) 1.23 (1.04-1.47, P = 0.02)) and risk of death within 10 years (RR 1.55 (1.50-1.61, P <0.001).[11,12]

From the results of echocardiography examination, there were significant differences in ejection fraction between mortality and survival group, whereas EF of patients who died was lower than those survival groups with EF 37.88 (4.34) versus 52 (13) with p: 0.001. This finding is similar with a
studied by Camara et al. aimed at identifying factors that could serve as a predictor of mortality within 1 year in patients with heart failure, the systolic dysfunction more common in the mortality group than the survival group (36.8% vs. 22.16%), and the probability of death within 1 year after the diagnosis of heart failure was 2.67 times higher in the group with EF <40% (Left ventricular ejection fraction / LVEF), OR 2.67, 95 % Confidence interval (CI) 1.36 - 5.23).14 This result is also consistent with a study conducted by Yin et al (2004) in a group of patients with hs-CRP > 2.97 mg / dl and EF <35 correlating significantly with MACE.[15]

The results of this study also showed differences in hs-CRP values between the mortality and survival group. The mean hs-CRP of the subjects who died within 90 days was 4.90 (1.68) while the mean hs-CRP in the non-dead subject within 90 days was 2.13 (1.62).

The statistical test using chi-square test, we found a differences hs-CRP value between mortality and survival subjects within 90 days in hospitalized heart failure patients (p:0.000). Previous studied of hs-CRP by Windram JD et al., which were followed for 36 months in patients with left ventricular systolic dysfunction had high hs-CRP values. As many as 163 (17%) of 957 patients died. Patients with a quartile value of hs-CRP > 11 pg / ml had the bad prognosis with HR 3.0 (2.1-4.1) p = <0.001.[16]

5. Conclusion
There are differences in hs-CRP values between in patients with heart failure who died and survival within 90 days.

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