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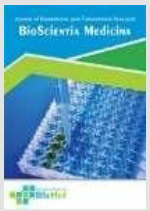

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The Relationship Between High-Sensitivity C-Reactive Protein (hs-CRP) and Diastolic Dysfunction in Geriatrics Patients at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

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A B S T R A C T

Background: Systemic inflammation associated with high hs-CRP levels constitutes one pathway through which diastolic dysfunction develops in older adults. This study aims to determine the relationship between high-sensitivity c-reactive protein (hs-CRP) and diastolic dysfunction in older adults at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia. **Methods:** This research is an observational analytical study using a cross sectional design. The research was conducted at the geriatrics polyclinic at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia from June to August 2023. A total of 65 people took part in this study. The relationship between hs-CRP and diastolic dysfunction was analyzed using SPSS version 25, univariate and bivariate. **Results:** Hs-CRP had a significant relationship with diastolic dysfunction on a numerical scale (p=0.012), with a median value of 1.6 mg/dL in subjects with diastolic dysfunction and 0.9 mg/dL in subjects without diastolic dysfunction. On the categorical scale, the hsCRP less than 1 mg/dL group found nine subjects (23.7%) with diastolic dysfunction and 14 subjects (51.9%) without diastolic dysfunction, the hsCRP 1-3 mg/dL group found 21 subjects (55.3%) with diastolic dysfunction and 12 subjects (44.9%) without diastolic dysfunction, in the hsCRP more than 3 mg/dL group (p=0.026) there were eight subjects (21.1%) with diastolic dysfunction and one subject (3.7%) without dysfunction diastolic. **Conclusion:** There is a significant relationship between hsCRP and left ventricular diastolic dysfunction in geriatrics patients at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

1. Introduction

Diastolic cardiac dysfunction is one of the cardiovascular health problems that is receiving increasing attention, especially among geriatrics. Diastolic disorders often do not cause noticeable symptoms in the early stages, but as we age, the risk of experiencing severe complications such as heart failure increases significantly. Therefore, it is essential to understand the factors that contribute to the development of diastolic dysfunction in old age. One factor that is increasingly recognized and receiving attention is high sensitivity C-reactive protein (hs-CRP). Hs-CRP is a biomarker used to measure systemic inflammation in the body.[1-5]

High hs-CRP levels have been linked to various chronic conditions, including heart disease. However, it is known that the relationship between hs-CRP and diastolic dysfunction in geriatrics is still a subject of growing research. Several recent studies have shown a correlation between high hs-CRP levels and a higher risk of diastolic dysfunction in old age. Diastolic dysfunction is a disturbance in the heart's relaxation phase when the ventricles (heart chambers) refill with blood. This disorder can cause various symptoms, including shortness of breath, fatigue, and an increased risk of heart failure. Research has shown that inflammation associated with high hs-CRP levels can affect heart structure and function, including changes in heart muscle tissue and changes in the elasticity of the heart walls. Other factors associated with diastolic dysfunction, such as high blood pressure, diabetes, and obesity, may also contribute to elevated hs-CRP levels. Therefore, it is theorized that systemic inflammation associated with high hs-CRP levels is one of the pathways through which diastolic dysfunction develops in the elderly population.[6-10] This study aims to determine the relationship between high sensitivity c-reactive protein (hs- CRP) and diastolic dysfunction in geriatrics at Dr. Mohammad Hoesin General Hospital Palembang, Indonesia.

2. Methods

This study is an observational analytical study using a cross-sectional design to assess the relationship of hs-CRP as an inflammatory marker to cardiac diastolic function. The research was conducted at the geriatric polyclinic at Dr. Mohammad Hoesin General Hospital, Palembang, from June to August 2023. A total of 65 people participated in this study, and the research subjects met the inclusion criteria. The inclusion criteria for this study were all patients seeking treatment at the geriatrics outpatient clinic aged ≥ 60 years old and willing to participate in the research and sign informed consent. This study has received ethical approval from the ethical committee of Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

This study made observations of high-sensitivity C-Reactive Protein (hs-CRP) levels. Hs-CRP is a marker of low-grade chronic inflammation that is widely used in predicting the incidence of cardiovascular events. Observation of heart performance in the form of diastolic function is carried out. Diastolic function was assessed using electrocardiography, where E/A < 0.8 in grade 1 diastolic dysfunction, E/A 0.8 – 2 with E/e' > 13 or LA dilatation was found in grade 2 diastolic dysfunction, E/A > 2 in grade 3 and 4 diastolic dysfunction. Data analysis was carried out using SPSS version 25 software. Data analysis was carried out univariate and bivariate. Univariate analysis was carried out to present the frequency distribution of each test variable. Bivariate analysis was carried out to determine the relationship between the test variables, where the p-value <0.05.

3. Results

In Table 1, it was found that 38 subjects were female (58.5%) and 27 subjects were male (41.5%); the average age of the research subjects was 70.37 $\pm$ 7.28 years. The age group > 70 years was 31 subjects (47.7%), and the < 70 years group was 34 subjects (52.3%). The average body mass index of participants was found to be 23.41 $\pm$ 4.26 kg/m^2, with a distribution of underweight as many as eight people (12.3%), normal body mass (BMI) index as many as 38 people (58.5%), overweight as many as 15 people (23.1%), and obesity as many as four people (6.2%). Low to middle education was 49 subjects (75.4%), and higher education was 16 subjects (24.6%). A smoking history was found in 13 participants (20%), while the rest did not smoke. Only six subjects (9.2%) regularly exercised >100 minutes per week, while 59 subjects (90.8%) exercised <100 minutes per week. The most common comorbidities found in research subjects were hypertension (63.1%), dyslipidemia (50.8%), osteoporosis (27.7%), chronic kidney disease (24.6%), diabetes mellitus (23.1%), and stroke (7.7%). The drugs most commonly consumed were ACEi/ARBs by 32 subjects.

Table 1. Participant's characteristics.

Characteristics	Total (n)	Percentage (%)
Gender		
Male	27	41,5
Female	38	58,5
Age (years old)	70,37 ± 7,28	
≥ 70	31	47,7
< 70	34	52,3
Body mass index (kg/m^2)	23,41 ± 4,26	
Normal	38	58,5
Overweight	15	23,1
Obesity	4	6,2
Underweight	8	12,3
Education		
Low to middle	49	75,4
High	16	24,6
Smoking history		
Yes	13	20,0
No	52	80,0
Exercise		
<100 minute/week	59	90,8
≥100 minute/week	6	9,2
Comorbid disease		
Hypertension	41	63,1
Diabetes mellitus	15	23,1
Chronic kidney disease	16	24,6
Dyslipidemia	33	50,8
Stroke	5	7,7
Osteoporosis	18	27,7
Medication		
ACE-inhibitor/ARB	32	49,2
Aspirin	8	12,3
Statin	17	26,2
Metformin	10	15,4
Vitamin D	11	16,9
Paracetamol	14	21,5
Edmonton frailty score		
Not frailty	41	63,1
Vulnerable	22	33,8
Mild frailty	2	3,1
Cognitive function (MMSE)		
None	57	87,7
Mild cognitive disturbance	6	9,2
Severe cognitive disturbance	2	3,1
Activity daily life (Barthel index)		
Independent	36	55,4
Mild dependency	27	41,5
Medium dependency	2	3,1

In Table 2, hsCRP levels have a median of 1.3 mg/dL, with the lowest value of 0.2 mg/dL and the highest of 8.5 mg/dL. Based on the AHA and CDC, hsCRP is grouped into three categories, namely < 1 mg/dL obtained by 23 subjects (35.4%), hsCRP 1-3 mg/dL obtained by 33 subjects (50.8%), and hsCRP > 3 mg/dL obtained by as many as nine subjects (13.8%). The total cholesterol value has a median of 187 mg/dL, with the lowest value being 105 mg/dL and the highest being 416 mg/dL. The LDL value has a median of 125 mg/dL, with the lowest value at 54 mg/dL and the highest at 249 mg/dL. The HDL value has a mean of 53.32 ± 11.87. Triglyceride values had a median of 121 mg/dL, with the lowest value 41 mg/dL and the highest 286 mg/dL. The mean eGFR was 67.70 ± 22.62. Echocardiographic parameters showed mean LVEDd 4.26 ± 0.61, mean IVSd 1.09 ± 0.15, mean LVPWd 0.97 ± 0.14, mean aortic diameter

3.35 ± 0.39, left atrial (LA) diameter mean 3.00 ± 0.52. Left ventricular mass index (LVMI) had a median of 91.7 g/m^2, with the lowest value of 51.9 g/m^2 and the highest of 143 g/m^2. Increased LVMI was found in 15 subjects (23.1%) and normal in 50 subjects (76.9%). The concentric remodeling type was the most common left ventricular geometry, with 29 subjects (44.6%).

Table 2. Overview of laboratory and echocardiography evaluation.

Characteristics	Total (n)	Percentage (%)
Laboratory evaluation		
hsCRP	1,3 (0,2 – 8,5)	
<1 mg/dL	23	35,4
1-3 mg/dL	33	50,8
>3 mg/dL	9	13,8
Total cholesterol	187 (105 – 416)	
LDL	125 (54 – 249)	
HDL	53,32 ± 11,87	
Trigliserida	121 (41 – 286)	
eGFR	67,70 ± 22,62	
Echocardiography		
LVEDd	4,26 ± 0,61	
IVSd	1,09 ± 0,15	
LVPWd	0,97 ± 0,14	
Ao	3,35 ± 0,39	
LA	3,00 ± 0,52	
LVMI	91,70(51,9 – 143)	23,1
Increased	15	76,9
Normal	50	
Left ventricle geometry		32,3
Normal	21	44,6
Concentric remodelling	29	12,3
Concentric hypertrophy	8	10,8
Eccentric Remodelling	7	
Left ventricle fraction ejection	75,15 ±7,08	

The results of the analysis in Table 3 show that hsCRP has a significant relationship with diastolic dysfunction both on a numerical scale (p=0.012) with a median value of 1.6 mg/dL in subjects with diastolic dysfunction and a median value of 0.9 mg/dL in subjects without diastolic dysfunction. On the categorical scale, the hsCRP <1 mg/dL group found nine subjects (23.7%) with diastolic dysfunction and 14 subjects (51.9%) without diastolic dysfunction, the hsCRP 1-3mg/dL group found 21 subjects (55.3%) with diastolic dysfunction and 12 subjects (44.9%) without diastolic dysfunction, in the hsCRP >3 mg/dL group (p=0.026) there were eight subjects (21.1%) with diastolic dysfunction and one subject (3.7%) without dysfunction diastolic.

Table 3. hsCRP and diastolic dysfunction.

Characteristics	Diastolic dysfunction (n=38)	No diastolic dysfunction (n=27)	P-value
hsCRP	1,6 (0,3 – 8,5)	0,9 (0,2 – 5,9)	0,012
<1 mg/dL	9 (23,7%)	14 (51,9%)	0,026
1 – 3 mg/dL	21 (55,3%)	12 (44,4%)	
>3 mg/dL	8 (21,1%)	1 (3,7%)	

4. Discussion

Diastolic dysfunction can be caused by cardiac fibrosis caused by increased collagen deposition in the interstitium which is partly mediated by inflammatory processes. Low-grade systemic inflammation is associated with high arterial stiffness, which in turn is associated with ventricular stiffening and diastolic heart failure. Diastolic dysfunction can be caused by various factors, including cardiac fibrosis which can be associated with increased collagen deposition in the interstitium (space between cells) of the heart. This is one mechanism that can cause heart stiffness and disturbances in the relaxation or diastolic phase. Inflammatory processes that contribute to increased hs-CRP levels may also contribute to the development of cardiac fibrosis. Chronic systemic inflammation can trigger structural changes in cardiac tissue, including increased collagen deposition. When collagen tissue increases, the heart can become stiffer and less elastic, which in turn can disrupt the normal diastolic process. Additionally, chronic inflammation can also impact the arteries by increasing arterial stiffness. Arterial stiffness can cause increased pressure on the heart's ventricles when they fill with blood (diastolic), which can cause impaired diastolic function. These disorders may then become risk factors for the development of diastolic heart failure. Thus, there is a complex relationship between systemic inflammation, cardiac fibrosis, arterial stiffness, and diastolic dysfunction in the heart.[11-15]

In this study, 38 subjects (58.4%) had diastolic dysfunction, with 24 subjects (63.2%) aged > 70 years. The relationship between variables that could be factors influencing the incidence of diastolic dysfunction in this study was analyzed using the Chi-square test. hsCRP >1.5mg/dL was found in 21 subjects (55.3%) with diastolic dysfunction, while hsCRP <1.5mg/dL was found in 6 subjects (22.2%) without diastolic dysfunction with a p value = 0.008. The results of this study indicate that hsCRP plays a role as a factor associated with diastolic dysfunction. The results of this study are in line with other studies which show that hsCRP is more closely related to left ventricular diastolic dysfunction than left ventricular hypertrophy after adjusting for confounding factors. Other studies show that hsCRP is closely related to left ventricular diastolic dysfunction. Other studies also show a significant relationship between hsCRP and diastolic dysfunction in patients who have cardiovascular risk factors.[16-19]

5. Conclusion

There is a significant relationship between hsCRP and left ventricular diastolic dysfunction in elderly patients at Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia.

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