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Relationship of Phase II Cardiac Rehabilitation Program with **Red Blood Cell Distribution Width Level in Post Coronary Artery Bypass Grafting Patients**

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Abstract : Background: Coronary heart disease is a chronic inflammation that is influenced by various factors. Increased levels of Red Blood Cell Distribution Width (RDW) are associated with an increase in cardiovascular mortality. Cardiac rehabilitation acts as an anti-inflammatory and improves risk factors. This study aims to assess the relationship of phase II cardiac rehabilitation programs with RDW levels in patients after Coronary Artery Bypass Graft (CABG).

Methods: This is a cohort study conducted from October 2018 to November 2018 with the study subjects is post-CABG patients undergoing phase II cardiac rehabilitation programs. RDW levels were examined in two measurement periods, before and after the cardiac rehabilitation program. The study observed changes in various parameters and analyzed the relationship between cardiac rehabilitation programs with RDW levels.

Result: We found changes on various parameter such as body weight, body mass index, six minute walking distance, functional capacity, RDW levels, glycated haemoglobin (HbA1c) levels, and Erytrocyte Sedimentation Rate (ESR) which was better and statistically significant with p <0.001. There was a strong negative correlation between RDW levels and functional capacity before (r -0.932; p < 0.001) and after the cardiac rehabilitation program (r -0.961; p < 0.001).

Conclusion: The phase II cardiac rehabilitation programs improving the RDW levels. Not only the RDW levels, but also other parameters such as HbA1c, ESR levels and functional capacity of patients after CABG. There is a negative correlation between the RDW levels and functional capacity both before and after the phase II cardiac rehabilitation program.

Keywords : cardiac rehabilitation, RDW, CABG.

Introduction

Cardiovascular disorders is a major health problem worldwide and contribute to high mortality and morbidity rates. Recent studies shown a strong relationship between increasing red blood cell distribution width (RDW) as a predictor of cardiovascular disorders.^{1,2,6}

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RDW is a quantitative measurement to assess anisocytosis, which shows the size variability of circulating red blood cells. In general high RDW level, indicate increasing damage to red blood cells. RDW is routinely examined in the complete blood count of all patients but is often ignored.^{6,7,12,14}

Research shows a strong association between high levels of RDW and the risk of cardiovascular events, regardless of classical risk factors. Increased RDW is associated with increasing red blood cells that bind oxygen incompletely. Increased RDW will affect oxygen transport capacity so that it can trigger adverse clinical events.^{12,15,16}

Cardiac rehabilitation is a coordinated intervention on various aspects designed to optimize heart patients in matters such as physical, psychological, and social functions, in addition to stabilizing, slowing down, or even reversing the progression of the atherosclerosis process, so that it may reduce morbidity and mortality. ^{1,2,8,9}

Cardiac rehabilitation programs in CAD patients will reduce proinflammatory cytokine production and induce the work of nitric oxide synthase and antioxidant effects that will increase erythroid proliferation in the bone marrow. In addition, the rehabilitation program will change the shape of erythrocytes, reduce the ratio of erythrocyte abnormalities and increase the concentration of 2,3-diphosphoglycerate in red blood cells thereby increasing oxygen transport.^{2,10,12}

Six minutes walking test (SMWT) is a simple, easy, accurate, high validity test that can be used to assess patient submaximal functional capacity. The aim of this study is to determine the relationship of phase II cardiac rehabilitation programs with RDW levels in post CABG patients undergoing phase II cardiac rehabilitation programs.^{2,3}

Methods

This study is a cohort study conducted from October 2018 to November 2018. A total of 30 post-CABG patients who would undergo cardiac rehabilitation, who met the inclusion and exclusion criteria were enrolled in this study. Inclusion criteria was post-CABG patients whom completed \geq 90% of phase II cardiac rehabilitation programs. Patients with diabetes mellitus, anemia (Hb <12g / dL) and hematological abnormalities, worsening symptoms of congestive heart failure, impaired renal function (GFR <60 ml / i), severe infection or inflammatory process were excluded. This study was approved by the Health Research Ethics Committee of the Medical Faculty of the University of North Sumatra and the Ethics Committee of the General Hospital. H. Adam Malik Medan.

Post CABG patient who underwent phase I cardiac rehabilitation were informed regarding the phase II cardiac rehabilitation. Once the patient permitted to go home then a written consent was gained. Later, the patient will come for a follow up through the out patient clinic for a pre measurement of the RDW level and initial SMWT. RDW levels were assessed through peripheral blood sampling using the Sysmex XN-1000 machine. SMWT was carried out before rehabilitation begins which was displayed in the form of Metabolic Euivalent of Tasks (METs). Then the patients began undergoing phase II cardiac rehabilitation programs at the rehabilitation and prevention unit of Adam Malik General Hospital, for 3 sessions per week for 4 weeks. The type of exercise was aerobic exercise such as heart gymnastics, walking leisurely, jogging on a treadmill, and pedaling a static bicycle. Each session was preceded by a warm-up movement and ended with cooling. Before and after the phase II cardiac rehabilitation procedure measurements of the patient's vital signs such as blood pressure, pulse and breathing frequency were measured. The duration of each session was 30 minutes and the type of exercise was adjusted to the patient's abilities. In addition to training activities, counseling once a week was performed, which includes discussing the progress of the rehabilitation process, the difficulties experienced by patients, recommendations on diet and lifestyle, and motivation to increase adherence to the program. During the phase II cardiac rehabilitation program, all examination and treatment given were recorded. After completing a phase II cardiac rehabilitation program, patients were recommended for program evaluation. Then another measurement of RDW and SMWT were performed. Patient were educated regarding the activities that are allowed and type of exercise recommended to be done at home.

All data in this study were processed using SPSS version 23. The Kolmogorov-Smirnov and Saphiro-Wilk tests were used to determine the normality of data distribution. Data presentations for categorical variables were presented in percentage (%) whereas numerical variables with normal distribution were presented in mean \pm SD. Numerical variables such as RDW, HbA1c, ESR, SMWT, body weight and BMI in the two groups, namely the group before and after the rehabilitation program were assessed by paired T test. The Pearson correlation test was used to assess the correlation between physical capacity and RDW levels. Statistically significant differences were defined as P values <0.05.

Result

There were 30 people included in the study. There were 3 female (10%) and 27 male (90%). The average age of the subjects participating in this study was 57.33 years. The average body mass index was 26.08 kg / m2. Subject with cardiovascular risk factors such as hypertension were 27 patients (90%) and 20 smoker (66.7%).

The average SMWT distance before the program was 192.97 meters. The average functional capacity of the subject before the program was 2.64 ± 0.42 METs. The average RDW level before the program was 13.70%, the average level of HbA1c was 6.15% and the average level of ESR before the program was 13.09 mm / hour.

Variable	Value
Female (n,%)	3 (10)
Male (n,%)	27 (90)
Age (years±SD)	57.33 ± 8.70
BMI (kg/m ² \pm SD)	26.08 ± 4.24
Hypertension (n,%)	27 (90)
Smoker (n,%)	20 (66.7)
SMWT (m±SD)	192.97 ± 74.13
Functional Capacity (METs±SD)	2.64 ± 0.42
RDW (%,±SD)	13.70 ± 0.72
HbA1c (%,± SD)	6.15 ± 0.63
ESR (mm/hour±SD)	13.09 ± 3.08

Table 1. Patient's Baseline Characteristics

Changes in Variables Before and After the Cardiac Rehabilitation Program

A statistical analysis was conducted to compare and assess changes in variables before and after phase II cardiac rehabilitation program. Table 2 shows differences in variables before and after the program.

There was a change in body weight which was statistically significant (p value <0.001) between groups, from 68.98 \pm 12.35 kg before the program to 67.03 \pm 11.52 kg after the program. There was a change in BMI as well that was statistically significant (p value <0.001) between groups, from 26.08 \pm 4.24 kg / m² before the program to 25.38 \pm 3.97 kg / m² after.

Table 2.	Changes in	Variables	Before and	After the	Cardiac	Rehabilitation	Program

	Before	After	P value
RDW (%,±SD)	13.70 ± 0.72	13.19 ± 0.66	< 0.001
HbA1c (%,± SD)	6.15 ± 0.63	5.7 ± 0.67	< 0.001
ESR (mm/hour±SD)	13.09 ± 3.08	7.47 ± 1.65	< 0.001
SMWT $(m \pm SD)$	192.97 ± 74.13	364 ± 128.99	< 0.001
Functional Capacity(METs±SD)	2.64 ± 0.42	6.6 ± 1.30	< 0.001
Body Weight (kg \pm SD)	68.98 ± 12.35	67.03 ± 11.52	< 0.001
BMI (kg/m ² ±SD)	26.08 ± 4.24	25.38 ± 3.97	< 0.001

Significant changes in SMWT were found (p <0.001) in both groups, from 192.97 ± 74.13 m before to 364 ± 128.99 m after the program. Significant changes in functional capacity (p <0.001) were found between the two groups, from 2.64 ± 0.42 METs before becoming 6.6 ± 1.3 METs after. Significant changes were also found (p <0.001) in RDW levels from $13.7 \pm 0.72\%$ before to $13.19 \pm 0.66\%$ after the program. In addition, there was a significant changes in the HbA1c level from $6.15 \pm 0.63\%$ to $5.7 \pm 0.67\%$ (p <0.001). Changes in the ESR level were also found significantly (p <0.001) which was 13.09 ± 3.08 mm / hour in the group before became 7.47 ± 1.65 in the group after.

Correlation between RDW and Functional Capacity

Table 3 showed a negative correlation between RDW levels and functional capacity before the program with a r value of -0.932 and p < 0.001, which is statistically a strong correlation.

Table 3. Correlation between RDW and Functional Capacity Before Phase II Cardiac Rehabilitation Program

RDW	r pearson	P value
Functional Capacity (METs)	- 0,932	<0,001

Table 4 showed a strong negative correlation between the RDW levels and functional capacity after the program with a r value of -0.961 and p < 0.001.

Table 4. Correlation between RDW and Functional Capacity After Phase II Cardiac Rehabilitation Program

RDW	r pearson	P value
Functional Capacity (METs)	- 0,961	<0,001

Discussion

This study aims to find a relationship between phase II cardiac rehabilitation programs with RDW levels. This study produces characteristic data and analysis of research subjects who can provide information, support, or refute theories that have been suggested from previous studies regarding the relationship between phase II cardiac rehabilitation programs with RDW levels and with other variables.

Overall the majority characteristics of the study subjects were male, smokers, had hypertension and overweight. Better changes were found and statistically significant on various parameters such as weight, body mass index, SMWT distances, functional capacity, RDW levels, HbA1c levels, and ESRs.

The results of this study indicate that RDW levels before and after the phase II cardiac rehabilitation program were found to be improved. In addition, there was an improvement in the functional capacity of patients after the cardiac rehabilitation program. These results were in accordance with previous studies conducted by Nishiyama, et al., Who assessed the effect of exercise on improving RDW levels as a predictor of improvement in functional capacity in CAD patients. This finding is also in line with Lavie et al's study of 235 obese CHD patients who were included in the heart rehabilitation program, which found improvements in body weight, BMI, exercise capacity, and quality of life.^{10,12,16}

In the study by Gwozdzinski et al., which assessed changes in post CABG patients who underwent cardiac rehabilitation for 2 months, a significant decrease in ESRs levels was found (P = 0.0245). This study also shows that cardiac rehabilitation not only improves metabolic parameters, but also exercise capacity, muscle strength, and inflammatory status.

Another study conducted by Lavie and Milani in women with post acute infarction showed an increase in functional capacity by 33% after undergoing a cardiac rehabilitation program.

According to a study conducted by Gayda et al., long-term cardiac rehabilitation in CAD patients has been shown to be effective in reducing metabolic syndrome, which in turn will also improve exercise tolerance. There were improvements in body weight, BMI, triglycerides, HDL levels, and insulin resistance.

In this study there was also a statistically significant decrease in HbA1c levels after cardiac rehabilitation program. This is in line with a previous study by Kim, et al., who found a significant improvement in the functional capacity of patients with or without DM after cardiac rehabilitation.

There was a negative correlation between RDW levels and functional capacity both before and after the cardiac rehabilitation program. This can be interpreted as if there is a decrease in RDW levels, then the functional capacity will increase and vice versa.

The results of this study turned out to be in accordance with previous studies conducted by Nishiyama, et al. The study was conducted in stable CAD patients who had been diagnosed with coronary angiography and functional capacity assessed by VO2 max obtained after patients were given exercise training using ergocycle. The results of the study showed that the cardiac rehabilitation would increase functional capacity and have a negative correlation with RDW levels, regardless of the CAD severity.^{10,13,16}

Limitation

The subject study is less compared to other studies and limited to post CABG patients who have taken phase II cardiac rehabilitation programs only. We only observed changes in RDW levels before and after the program, without further follow up regarding the long-term effects and the presence of major cardiovascular events such as rehospitalization in these patients.

Conclusion

The phase II cardiac rehabilitation programs improving the RDW levels. Not only the RDW levels, but also other parameters such as HbA1c, ESR levels and functional capacity of patients after CABG. There is a negative correlation between the RDW levels and functional capacity both before and after the phase II cardiac rehabilitation program.

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