Right Ventricular Function and Exercise Tolerance in Patients with ST-Elevation Myocardial Infarction

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Abstract

Background: Following ST-segment elevation myocardial infarction (STEMI), patients with cardiac dysfunction have limitations in performing physical activity. Right ventricular (RV) function is a determinant in improving functional capacity, and cardiac rehabilitation (CR) is essential for this patient cohort.

Objective: To evaluate the association of RV function with exercise tolerance after a CR program in patients with STEMI.

Methods: Retrospective cohort study in patients with STEMI from January to December 2019. They underwent an echocardiographic assessment of RV function before a 16-session CR program. A cardiopulmonary exercise (CPX) testing was performed before and after the CR program. We analyzed whether RV function measured before CR was significantly associated with exercise tolerance before and after the CR program and the degree of improvement. Comorbidity, demographic and anatomic variables were documented. A p-value < 0.05 was considered statistically significant.

Results: A total of 109 patients were included. Of all, 3.7% had global RV dysfunction, 10.1% had radial RV dysfunction, and 11% had longitudinal RV dysfunction. An association between radial or longitudinal RV dysfunction and the absence of improvement in cardiorespiratory fitness (> 1 peak VO₂ equivalents) was observed (p = 0.028, p = 0.008, respectively). A significant correlation was observed between longitudinal RV dysfunction with initial peak VO₂ equivalents (pVO₂ eq) (p = 0.046), final pVO₂ eq (p = 0.003), and difference in pVO₂ eq (p = 0.009). A correlation was also identified between global RV dysfunction and the initial pVO₂ eq (p = 0.045), final pVO₂ eq (p = 0.012), and difference in pVO₂ eq (p = 0.032).

Conclusions: RV dysfunction is associated with a lower capacity to exercise; CR programs can be extended or modified in these patients.

Keywords: Cardiac Rehabilitation; ST Elevation Myocardial Infarction; Echocardiography; Ventricular Function.
Therefore, the primary objective of this study was to evaluate the association of RV function with exercise tolerance after a CR program in patients with STEMI treated with percutaneous coronary intervention. Secondary objectives were to analyze RV function parameters and ventricular dysfunction frequency before CR and compare metabolic equivalents of oxygen consumption (pVO$_2$eq), representing cardiorespiratory fitness and functional class between patients with and without longitudinal, radial, and global RV dysfunction.

**Methods**

This study was an analytical retrospective cohort.

**Study population**

We retrospectively reviewed CR clinical records of 109 adult male and female patients with STEMI. All of them were treated with percutaneous coronary intervention in the UMAE Hospital of Cardiology No. 34 IMSS in Monterrey, Nuevo León, Mexico, from January 1, 2019 to January 30, 2020. Transthoracic echocardiography was performed only before CR. A cardiopulmonary exercise (CPX) testing was scheduled before and after CR. Comorbidities were recorded when diabetes mellitus, hypertension, smoking, and dyslipidemia coexisted. Exclusion criteria were: absence of echocardiographic data before CR, patients with STEMI but without a CR program, the dropout from CR, absence of CPX findings before and after CR, other types of myocardial infarction (type 2, 4, and 5), and non-STEMI.

**Echocardiography**

Systolic LV function and RV function were evaluated using Vivid 9 and Vivid E95 General Electric® equipment for resting transthoracic echocardiography only before CR, measuring left ventricle ejection fraction (LVEF) and RV fractional area change (RVFAC), tricuspid annulus systolic excursion (TAPSE) and tissue Doppler systolic velocity (S’ wave) of the tricuspid annulus. Based on the American Society of Echocardiography guidelines, LV dysfunction was defined as LVEF < 50%. To accurately detect RV dysfunction, we determined whether it is characterized by longitudinal RV dysfunction using one or more of the following criteria: TAPSE < 1.8 cm or S’ wave < 9.5 cm/s. Radial RV dysfunction was defined as RVFAC < 35% and global RV dysfunction if two or more previous measurements were available.

**Cardiopulmonary exercise testing**

CPX was performed on a General Electric® T2100ST1 treadmill with CASE software before and after the CR program to establish initial and final cardiorespiratory fitness. The CR program was performed on a recumbent Ergoline® GmbH ergometer with approximately 10 W/min workload increments every 5 minutes until the subjects achieved the criteria for test termination (angina,
ST segment change, dyspnea, exhaustion, hypotension) or completed 40 minutes on the treadmill. In total, 15 to 20 sessions were completed by patients, depending on their specific situation. Continuous measurement of pVO₂ eq was carried out.

The Research Ethics Board of the UMAE Hospital of Cardiology No. 34 IMSS approved the study, according to article 17 of the section on Ethical Aspects of Human-Subject Research of the General Health Law Research Regulations in Mexico. This protocol corresponds to a research study without risk, involving reviewing clinical records, in which no sensitive aspects of a patient’s behavior were identified or treated.

**Statistical analysis**

Descriptive statistics were calculated with frequency and percentage for nominal variables. For continuous variables, mean, standard deviation, median, and interquartile range were reported according to data normality. Preliminary analyses showed that most of these variables were not normally distributed, as assessed by the Kolmogorov-Smirnov test (p < 0.05). The exceptions were the variables age and RVFAC, which had a normal curve distribution (p = 0.131, p = 0.200, respectively). Inferential analysis of continuous variables was performed according to the normal distribution curve. Statistical significance was considered when p < 0.05. The difference in cardiorespiratory improvement in pVO₂ eq before and after CR was assessed by the Wilcoxon test. The association between (longitudinal and radial) RV function and change in cardiorespiratory fitness (> 1 pVO₂ eq) in CPX after CR was assessed with Fisher’s exact test.

Kendall’s tau-b was used to assess the relationship between global and longitudinal RV function with initial pVO₂ eq, final pVO₂ eq, and the difference in pVO₂ eq (p < 0.05). Spearman’s Rho test was conducted to determine the correlation between LVEF and final Functional Class, and initial pVO₂ eq (p < 0.05). Statistical analysis was performed using standard statistical software packages (SPSS software 25.0; SPSS Inc, Chicago, IL, USA, and Office Excel; Washington, USA).

**Results**

We included 109 patients. Demographics and STEMI characteristics are shown in Table 1. Most of the patients were men, hypertensive, and with dyslipidemia. They had a median LVEF of 49%, with a median CAF of 45% of radial RV function. A low percentage of patients had radial, longitudinal, and global RV dysfunction (Table 1).

The most common site of infarction was anterior, followed by inferior ones. Regarding the CR program, there was a considerable improvement in pVO₂ eq. The median change in cardiorespiratory fitness before and after CR was 2.1 pVO₂ eq, the difference being significant (Z = -9.02 p = 0.001).

Most patients completed the rehabilitation program in New York Heart Association (NYHA) functional class 1, and most patients had an LVEF of more than 40%. Central Illustration.

A statistically significant difference was observed comparing patients with or without radial RV dysfunction and the presence of improvement in cardiorespiratory fitness (> 1 pVO₂ eq) (p = 0.028). The difference between comparing patients with or without longitudinal RV dysfunction and improvement in cardiorespiratory fitness was also significant (p = 0.008) (Table 2). Another significant difference was observed between patients with or without radial RV dysfunction and the presence of improved NYHA functional class (p = 0.031).

RV FAC had a significant negative correlation with improvement in cardiorespiratory fitness (r = -0.216 p = 0.010). Longitudinal and global RV dysfunction had significant negative correlations with initial pVO₂ eq, final pVO₂ eq, and improvement in pVO₂ eq. LVEF had a significant correlation with initial pVO₂ eq and with final NYHA functional class (Table 3, Figures 1 and 2).

**Discussion**

The main findings of the present study are that longitudinal and radial RV dysfunction are associated with worse cardiorespiratory fitness after CR in patients with STEMI treated with primary PCI. In previous studies, Tajima et al. documented that global RV function significantly determines exercise capacity in ischemic heart disease before CR. Nevertheless, the patients included were heterogeneous with multivessel coronary artery disease treated with PCI or coronary artery bypass surgery. In our study, basal echocardiography also showed this association.

We found that radial RV dysfunction, evaluated as FAC, was associated with a lack of improvement in cardiorespiratory fitness (> 1 pVO₂ eq); this suggests that radial RV fibers are involved in the functional capacity of these patients. The observation that initial, final, and improvement of pVO₂ eq showed correlations with longitudinal and global RV dysfunction is consistent with other studies that showed this relationship between RV dysfunction and poor exercise tolerance, a fact related to ventricle-pulmonary artery uncoupling. Legris et al. observed that in patients with heart failure, RV dysfunction assessed using FAC and myocardial performance index was associated with exercise tolerance studies; however, longitudinal function did not show this relationship. These findings reflect the preload-dependent conditions of this method.

Many studies have compared RV function in patients with ischemic heart disease undergoing CR, using echocardiographic measurement of TAPSE and S’ velocity. In patients treated with coronary artery bypass grafts, a reduction in these parameters to at least half of normal values seems to be a typical feature of uncomplicated cardiac surgery. This reduction has been related to the opening of the pericardium, changes during CPB, and sternotomy. Still, it does not necessarily indicate impairment of RV function, and these changes persist for 12 to 24 months. For this reason, we only enrolled patients undergoing percutaneous treatment.

Only 33% of the patients had right coronary artery disease; these results suggest that RV dysfunction is not only related to multi-vascular disease or right coronary artery disease but is also an independent entity with a poor prognosis once it is present. Previous studies reported such findings in patients with acute myocardial infarction and cardiogenic shock with and without left anterior descendant coronary artery disease.
The results of this study suggest that although there is an improvement in functional class and V\textsubscript{O}\textsubscript{2} consumption in these patients, RV dysfunction is associated with a lower response to exercise tolerance in CR programs. They also show that RV dysfunction persists after CR and possibly has future repercussions.

Nevertheless, in our study, all patients improved in functional class and V\textsubscript{O}\textsubscript{2}; this was reflected in the difference in pV\textsubscript{O}\textsubscript{2},eq, with a maximum of 3.8. Patients with RV dysfunction, both longitudinal and radial, showed improved cardiorespiratory fitness (> 1 pV\textsubscript{O}\textsubscript{2},eq) at the end of CR. Therefore, these patients probably acquired the benefits previously recognized in other studies where improvement by one V\textsubscript{O}\textsubscript{2} equivalent decreased mortality by 25%\textsuperscript{19}. These findings suggest that RV dysfunction decreases the capacity to respond to physical activity; however, this does not entirely limit the benefits of CR. Moreover, this population may benefit more from an extended program or different exercise routines to improve their functional class. These programs positively affect selected patients even with the limitations mentioned. This situation was addressed in the study by Ohara et al.; they found that patients with low TAPSE who underwent CR for six months improved their functional class, reduced B-type natriuretic peptide levels, reduced afterload of the right ventricle and improved left ventricle systolic function even though the TAPSE did not change in a final echocardiographic study. The results suggest that a more extended CR strategy could improve the cardiorespiratory fitness of these patients\textsuperscript{14}.

As reported previously, LVEF correlated with functional class and initial pV\textsubscript{O}\textsubscript{2},eq. LV dysfunction is related to exercise intolerance because of the impaired systolic reserve, which further impairs stroke volume reserve during stress\textsuperscript{20}.

The benefit of CR is reflected in the fact that 86% of the patients finished the CR program in functional class I, with an average improvement of 2.4 pV\textsubscript{O}\textsubscript{2},eq ≥ 1.4; only 12.5% ended up in functional class II and 0.9% in class III. This data was studied previously in patients with heart failure, and similar results were found with TAPSE.\textsuperscript{14} Therefore, RV dysfunction is associated with a lower exercise tolerance capacity; nevertheless, this does not reduce the benefits of rehabilitation programs for these patients.

The most appropriate rehabilitation strategies should be established for these patients. RV function parameters can help to characterize lower exercise tolerance and individualize the program to obtain the best short-term and probably long-term results.

Among the limitations of this study is the low frequency of patients with longitudinal, radial, and global RV dysfunction. Another limitation is that the total duration of each rehabilitation session was not considered, although the maximum time for each session was 40 minutes. The patient’s direct oxygen consumption was not measured, nor was the session suspended for any reason since only patients with a complete CR program were included; the underrepresentation of women was another bias factor.

Further studies are needed in which the follow-up of these patients is included in addition to the evaluation of oxygen consumption in correlation with exercise tolerance and RV function, as well as assessing long-term outcomes.

**Conclusions**

RV dysfunction in patients with ischemic heart disease with previous STEMI and primary percutaneous coronary intervention is associated and correlates with lower exercise tolerance and functional class before CR. After CR, the final pV\textsubscript{O}\textsubscript{2},eq was improved.
Table 2 – Association between functional class and radial/longitudinal RV dysfunction

<table>
<thead>
<tr>
<th>CF Improvement (&gt; 1 pVO₂eq)</th>
<th>Yes</th>
<th>No</th>
<th>N Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>83</td>
<td>15</td>
<td>98</td>
</tr>
<tr>
<td>Dysfunction</td>
<td>6</td>
<td>5</td>
<td>11</td>
</tr>
</tbody>
</table>

Fisher Test p = 0.028

Radial RV Function

Longitudinal RV Function

Fisher Test p = 0.008

CF: cardiorespiratory fitness; N: number of patients; RV: right ventricle; pVO₂eq: metabolic equivalents of oxygen consumption.

Table 3 – RV function parameters versus cardiovascular fitness parameters

<table>
<thead>
<tr>
<th>Variables</th>
<th>Correlation Coefficient (p-value)</th>
<th>Final NYHA FC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial pVO₂eq</td>
<td>Final pVO₂eq</td>
</tr>
<tr>
<td>Longitudinal RV dysfunction</td>
<td>tb = 0.159 (0.046)</td>
<td>tb = 0.238 (0.003)</td>
</tr>
<tr>
<td>Global RV dysfunction</td>
<td>tb = 0.160 (0.045)</td>
<td>tb = 0.201 (0.012)</td>
</tr>
<tr>
<td>LVEF</td>
<td>p = 0.200 (0.036)</td>
<td></td>
</tr>
</tbody>
</table>

Initial pVO₂eq: oxygen consumption in metabolic equivalents in initial CPX; final pVO₂eq: oxygen consumption in metabolic equivalents in the final CPX; improvement in pVO₂eq: difference of oxygen consumption in metabolic equivalents between initial and final CPX; NYHA FC: New York Heart Association Functional Class; tb: Kendall’s Tau-B correlation; LVEF: left ventricle ejection fraction; p: Spearman’s Rho correlation.

Figure 1 – Correlation between Longitudinal RV Dysfunction and Improvement in pVO₂eq. IQR: interquartile range; peak VO₂eq: peak VO₂ equivalents of patients with and without RV longitudinal dysfunction.

Author Contributions

Conception and design of the research and Writing of the manuscript: Guzman-Ramirez D, Trujillo-Garcia A; Acquisition of data: Trujillo-Garcia A, Lopez-Rincon M, Botello-Lopez R; Analysis and interpretation of the data and Statistical analysis: Guzman-Ramirez D; Critical revision of the manuscript for important intellectual content: Guzman-Ramirez D, Lopez-Rincon M, Botello-Lopez R.

Potential conflict of interest

No potential conflict of interest relevant to this article was reported.
Figure 2 – Correlation between RV Global Dysfunction and Final \( \text{pVO}_2 \) eq. IQR: interquartile range; \( \text{peak VO}_2 \) eq: \( \text{peak VO}_2 \) equivalents of patients with and without RV global dysfunction.

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**Study association**

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**References**


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