

Title: A research on the role of recovery methods in the reduction of ventricular remodeling post-acute myocardial infarction.

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Introduction: Myocardial Infarction (MI), commonly known as 'heart attack', is the principal cause of heart failure in the adult population. The mortality rate of patients who suffer MIs remains high even among the patients who have survived the acute phase of MI.

The objective of this doctoral research project is to demonstrate the role of initiating early patient mobilization post-Myocardial Infarction in the improvement of the patients' clinical evolution. In the first study, the biological and inflammatory markers associated with early mobilization were observed. The second study focused on the correlations between angiology aspects and early mobilization through the prism of complications arising at the post-intervention stage and during hospital admission. More specifically, the study observed the correlations between the type of MI and the severity of coronary lesions, on the one hand, and the rate of cardiac mobilization, on the other hand. In the third study, patients' evolution post-MI was observed, a month after the acute event, by using MRI examination for the complex evaluation of ventricular kinetics and remodelling as well as the extent of myocardial necrosis, in order to study the impact of early mobilization post-MI on the ventricular function and remodelling in patient evolution.

General Methodology: A number of 81 patients with Acute Myocardial Infarction (AMI) were observed, who were admitted to the Cardiology Department of the Emergency and Clinical County Hospital Tîrgu-Mureş. The patients were divided into two groups, depending on the day in which mobilization took place post-AMI. The first group was made up of the patients who were mobilized in the first 2 days post-AMI (n=30) and the second group consisted of patients who were mobilized after 3 days post-AMI (n=51). The average age for the first group was 54.80 ± 13.49 (1.69-4.08), and for the second group, it was 65.84 ± 12.31 (62.38-69.31), $p=0.0003$. The average weight of the patients in the first group was 83.67 ± 17.16 kg (77.26-90.07) and for the second group of patients, it was 82.51 ± 19.56 kg (77.01-88.01), $p=0.3$. The first group included 7 (23.33%), male patients, while the second group included 23 (45.89%), $p=0.005$. In the first group, there were 23 (76.66%) female patients and the second had 28 (54.9%), $p=0.005$. The average systolic blood pressure in the first group was 135.8 ± 19.51 (128.5-143.1) and 126.1 ± 19.36 (120.6-131.6) for the second group, with $p=0.1$. As regards the average diastolic blood pressure, for the first group it was 79.47 ± 12.95 (74.63-84.30) whilst for the second group it was 73.76 ± 12.15 (70.31-77.21), with $p=0.1$. The average pulse in the first group was 79.68 ± 15.56 (73.64-85.71) and 76.63 ± 14.06 (72.67-80.58) for the second group, with $p=0.3$.

Substudy 1: Biological and inflammatory markers associated with early mobilization

Objectives: This substudy aimed to investigate the link between the period of time until patient mobilization post-AMI and the biological and inflammatory markers, recorded for patients who undertook early mobilization (1-2 days post-AMI) compared to late mobilization (3-4 days post-AMI).

Material and Method: The inflammatory markers chosen for both groups were hs-CRP initially (first day of hospital admission) and after mobilization. The biomarkers were the usual ones with the addition of those that reflect myocardial necrosis and nutritional status.

Results: The average hs-CRP value post-MI was 5.34 ± 13.75 (1.69-4.08%) for group 1 and 19.47 ± 30.28 (10.87-28.08) for group 2, the difference being statistically significant: $p < 0.0001$. A week after MI, the

average hs-CRP values for the first group were 7.44 ± 7.82 (4.52-10.37), and 35.28 ± 38.74 (24.38-46.18) for the second group, with a difference of $p < 0.0001$. The values of the Prognostic Nutritional Index (PNI) were 58.5 ± 15.36 (52.76-64.23) in the first group and 49.03 ± 6.965 (47.07-50.99) in the second group ($p = 0.001$). In the first group, there was no patient in a severe stage of malnutrition (score 4 or 5 on the CONUT Index) and only one patient had a score of 3 on the CONUT Index. In the second group, 33% of the patients had a score higher than 3 on the CONUT Index, among which 15.68% had a score of 4 or 5 on the CONUT Index.

Conclusions: For patients with Myocardial Infarction, late mobilization in the period immediately following AMI is associated with higher values of myocardial necrosis enzymes, a more accentuated inflammatory status and poorer nutritional status.

Substudy 2: Correlations between the angiographic aspect, clinical evolution and post-AMI evolution

Objectives: This substudy was aimed at analyzing the correlation between the cardiac angiographical aspects post-AMI, particularly the localization of the necrotic lesion, and the amount of time until mobilization of the patients who suffered an AMI.

Results: The localization of stenoses at the level of the left artery's trunk was identified in 16.66% of the patients from the first group and 21.56% of the patients in the second group ($p = 0.6$). Stenoses at the level of the anterior descending artery were identified in 20 (66.66%) of the patients in the first group and 32 (62.74%) of the patients in the second group ($p = 0.8$). At the level of the circumflex artery, significant stenoses were identified in 12 (40%) of the patients in the first group and 26 (50.98%) of the patients in the second group, with a difference of $p = 0.2$, statistically insignificant. Stenoses at the level of the right coronary artery were identified in 36.66% and 47.05% of the first and second group, respectively, with a difference of $p = 0.2$, being statistically insignificant.

Conclusions: The angiographic aspect does not present a significant correlation with the rapidity of mobilization in the period immediately after MI, both when it comes to the culprit lesions and when looking at the angiographic aspect as a whole. The severity of coronary disease does not have a strong impact on the decision for mobilization, except for the case in which this is associated with the impairment of ventricular function.

Substudy 3: The impact of early mobilization on the extent of the infarction and the evolution a month post-MI

Objectives: This study proposed the investigation, with the help of cardiovascular magnetic resonance imaging (cardiac MRI), of patients who previously suffered an Acute Myocardial Infarction (AMI). This was conducted by performing an MRI examination a month after the acute event, with the purpose of identifying the differences between the patients who mobilized early (1-2 days) and those who mobilized late (after 3 days).

Results: The volume of the infarcted tissue was significantly higher for the patients with late mobilization: 15.11 ± 3.82 (13.68-16.54) in the first group and 35.83 ± 21.86 (29.68-41.98) in the second group ($p = 0.0001$). The infarcted tissue mass was also significantly higher in the late mobilization group, being 35.18 ± 24.76 (28.21-42.14) compared to 19.03 ± 5.09 (17.12-20.93) in the early mobilization group, resulting in a difference of $p = 0.001$ which is significantly higher. The percentage of myocardial infarction for the first group was 12.62 ± 3.46 (11.33-13.91), whilst for the second group, it was 22.31 ± 10.69 (19.31-25.32), observing a difference of $p < 0.0001$. The degree of infarct transmural was 7.75 ± 6.03 (5.5-10.01) for the first group and 29.20 ± 23.34 (22.64-35.76) for the second group, the correlation being statistically highly

significant (< 0.0001). The volume of the tissue presenting high transmural, measured in grams, was 8.14 ± 6.33 (5.78-10.51) for the first group and 30.70 ± 24.67 (23.76-37.64) for the second group ($p < 0.0001$).

Conclusions: Late-mobilized patients post-MI show a more severe evolution of the ventricular function, as evidenced by the MRI examination a month after MI. Therefore, the patients mobilized after more than 3 days from the start of the MI, showed a tendency for ventricular remodelling, a higher volume and mass of infarcted tissue, a reduced ejection fraction, a higher percentage of myocardial necrosis reported to the whole of the myocardial tissue and a higher degree of scar tissue transmural. These differences are evidenced both in the comparison between the groups as well as in the intra-group analysis, which revealed a tendency of aggravation of these parameters with every delayed day until mobilization.