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LONG NON-CODING RNAs IN ACUTE MYOCARDIAL INFARCTION RELATED TO HYPERCHOLESTEROLEMIA

By

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Summary and Conclusion

As Acute myocardial infarction is the first leading cause for mortality all over the world and with a high percent especially in Egypt. AMI is recognized by necrosis of cardiac myocytes with elevation in serum cardiac troponin. Also, it was said that AMI is related with familial hypercholesterolemia that famous with increase in levels in LDL-cholesterol and total cholesterol. Early detection of acute myocardial infarction decreases the death percentage and help in treatment of these cases. Unfortunately, traditional methods used in diagnosis of AMI as measuring levels of myocardial proteins for example: serum CK-MB, cardiac myoglobin and troponin. These biomarkers give false elevations results in other diseases not only AMI as in skeletal muscle injury and chronic renal failure. Recently, searching for new novel biomarkers for early diagnosis of acute myocardial infarction with high sensitivity and specificity become the most important point of research. Studying the effect of the expression of serum non-coding RNAs (LncRNAs and MicroRNAs) is a point of interest after many findings that give a relation between their expression and the cardiovascular diseases.

Therefore, this study is designed to explore new novel markers selected for serum non-coding RNAs (micro-RNAs and long non-coding RNAs) using in silico data analysis based on putative interactions between RNAs in AMI and to evaluate their usefulness as non-invasive diagnostic markers for AMI related with familial hypercholesterolemia.

This was an observational study in which 110 participants were enrolled. The first group consists of 35 AMI patients who recruited from recruited from Ain Shams University Hospital with acute and ongoing chest pain for 8 hours, with elevated serum cholesterol and evidence of familial hypercholesterolemia between January 2019 to January 2020. Another examined group contains 30 AMI patients without evidence of familial hypercholesterolemia. Additionally, 20 of non-cardiac patients who were suffering from chest pain but after examination and some analytical tests, they were diagnosed as non-cardiac chest pain. Finally, 25 healthy volunteers were served as a control group.

All subjects were subjected to:

- Full history and clinical examinations.
- Determination of relative miRNA-197, miRNA-221 and LncRNA_FENDRR expression levels in sera of all groups.

The results of the study can be summarized as follows:

- For lipid profile:
 - Compared to the control group, the levels of serum total cholesterol, serum triglycerides and serum LDL was elevated significantly in AMI patients' groups.
 - While there was a decrease in serum HDL level in AMI patients compared with control group with no significance.
- For cardiac markers:
 - Comparing with the control group, there was a high significance elevation of serum CK-MB and serum troponin T levels in the AMI patients' groups.
 - There was no significance between the two patients' groups with AMI (hypercholesteremic and non- hypercholesteremic) in levels of serum CK-MB and serum troponin.
- For studied serum non-coding RNAs:
 - For LncRNA_FENDRR and miRNA-221, there was high significance decrease in the expression of them in the AMI patients' groups compared with the control and non- cardiac groups.
 - A highly significance elevation in the expression of miRNA-197 in the AMI patients' groups regarding to the control and non-cardiac groups.
 - No statistical significance difference in the expression of LncRNA_FENDRR, miRNA-221 and miRNA-197 within the two patients' groups with AMI (hypercholesteremic and non-hypercholesteremic).
- The relative expression levels of LncRNA_FENDRR and miRNA-221 were significantly downregulated in the AMI group compared with the healthy volunteers while miRNA-197 expression levels showed significance upregulation.
- In the AMI patients' group, there was a significance negative correlation between the expression of LncRNA_FENDRR and the levels of serum CK-MB and serum troponin.
- A significance positive correlation between the expression of with the expression of LncRNA_FENDRR and the expression of miRNA-221 in the AMI group.
- ROC curves of the circulating expression levels of LncRNA_FENDRR, miRNA-221 and miRNA-197 to discriminate AMI patients from control group 'healthy control and non- cardiac groups' showed that miRNA-221 had the strongest diagnostic value for AMI with an area under curve of 0.955 and an optimal cut-off point of 2.56 followed by miRNA-197 with AUC of 0.950 with

a cut-off point of 1.334. On the other hand, the LncRNA_FENDRR showed AUC of 0.944 at a cut-off point of 1.94.

In summary, this study pointed out that expression of LncRNA_FENDRR, miRNA-221 and miRNA-197 in sera of Egyptian AMI patients can be considered as new novel biomarkers for early AMI diagnosis despite troponin levels lower than the detection limit.