Role of MicroRNA-1 as Diagnostic and Differentiating Biomarker between Acute Anterior Myocardial Infarction and Unstable Angina

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Abstract
Worldwide, coronary artery disease (CAD) accounts for a disproportionate share of all cardiovascular deaths. Disruption of the atherosclerotic plaque and thrombotic blockage of the artery cause acute coronary syndrome (ACS), a subtype of coronary artery disease (CAD). Acute anterior myocardial infarction (MI) and unstable angina (UA) are disorders that are part of acute coronary syndrome (ACS). These diseases indicate myocardial damage and necrosis. Assessment of symptoms, changes in troponin, and electrocardiogram (ECG) abnormalities due to ischemia are the current clinical diagnostic tools for acute coronary syndrome (ACS). On the other hand, “classic” symptoms are rare and don’t reliably differentiate between cardiac and noncardiac reasons of chest discomfort in certain groups, such as diabetics, women, and the elderly. Ultimately, miR-1 enhances myoblast development by targeting the production of heat shock proteins (HSP) -60, HSP-70, and Bcl-2. It is secreted into the bloodstream after cardiac damage and is strongly expressed in skeletal muscle and cardiomyocytes. Its promise for quick diagnosis is supported by the fact that its level rises in plasma samples taken from patients shortly after symptoms begin.

A number of diseases and conditions, including cardiovascular disease, have miRNAs in circulation as potential non-invasive indicators (CVD) The goal of this study was to identify if microRNA-1 could be utilised as a tool for discriminating between unstable angina (UA) and acute anterior myocardial infarction (MI), as well as to evaluate the impact of microRNA-1 expression in the diagnosis of UA and MI in patients (UA).

Keywords: unstable angina pectoris, microRNA-1, and acute anterior myocardial infarction.

1.Introduction

Coronary artery disease (CAD) accounts for a disproportionate share of all cardiovascular deaths. Disruption of the atherosclerotic plaque and thrombotic blockage of the artery cause acute coronary syndrome (ACS), a subtype of coronary artery disease (CAD) [1].

Myocardial damage and necrosis are symptoms of acute coronary syndromes (ACS), which include unstable angina (UA) and acute anterior myocardial infarction (MI) [2].

The basic causes of atherosclerotic plaque rupture and subsequent thrombosis are the same as previously stated [3]. Aclutely reduced blood flow in the coronary circulation is a result of this thrombus [4]. A number of variables increase the risk of coronary artery disease (ACS) [5]. These include smoking, high blood pressure, diabetes, high cholesterol, being male, not getting enough exercise, having a family history of the disease, being overweight, not eating well, and abusing cocaine. Almost twenty years ago, cardiac troponins I and T were the gold standard for diagnosing acute coronary syndrome. However, these markers are raised in patients suffering from myocarditis, aortic dissection, pulmonary embolism, congestive heart failure, and renal failure. Additionally, early biomarker-based detection of ACS is hindered since cardiac troponins are often generated from injured myocardial 4 to 8 hours after symptoms start [6]. So, finding new biomarkers could help detect ACS earlier, especially in those who have unusual symptoms of the disease [7].

Endogenous microRNAs (miRNAs) are single-stranded RNAs that are 19–24 nucleotides long and do not code [8]. Protein synthesis and translation are inhibited when these posttranscriptional regulators attach to the 3’ untranslated region (UTR) of the target gene, destabilising the mRNA and depressing translation [9].

AMI and coronary artery disease (CAD) are among the several disorders linked to dysregulation of microRNAs (miRNAs), which are essential for homeostasis [10]. It is common to find miR-1 and miR-133 in all kinds of CAD. They have important functions in cardiac physiology and are highly expressed there [11].

Ultimately, miR-1 enhances myoblast development by targeting the production of heat shock proteins (HSP)-60, HSP-70, and Bcl-2. It is released into the blood upon cardiac damage and is abundantly expressed in skeletal muscle and cardiomyocytes [12]. Its promise for quick diagnosis is supported by the fact that its level rises in plasma samples taken from patients less than 2 hours after the start of symptoms [13].

Cardiovascular disease (CVD) is one of the diseases that may be detected non-invasively by measuring miRNAs in the blood and other bodily fluids [14].

At present, miRNAs in circulation are being studied as potential non-invasive diagnostic indicators of cardiovascular diseases, such as unstable angina, ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and coronary artery disease (CAD and ACS)[15].

The stability of miRNAs in circulation makes them a promising biomarker candidate[15]. They are also resistant to ribonuclease.

2.Subject and Methods

Forty participants, forty from the Cardiology Department’s Coronary Care Unit at Benha University Hospital, and twenty from a healthy control group
participated in the study after it had been approved by the Research Ethical Committee of the Benha Faculty of Medicine and all participants had given their written informed consent. Twenty healthy individuals who were age and sex matched served as volunteers, whereas twenty patients suffering from unstable angina and twenty patients suffering from acute anterior myocardial infarction served as subjects (AMI). The blood: After collecting blood in an EDTA tube, it was divided into several portions and transferred to an RNase-free tube. The entire blood and plasma samples were kept at a temperature of -80°C until the RNA was extracted.

Estimation of miRNAs expression levels according to the following steps:
1. Total RNA including microRNA extraction.
2. Relative quantitation of microRNA-1 by two-step quantitative Real time PCR.
3. Data analysis.

3. Analytical synthesis

Version 20.0 of IBM's statistical programme for social science (SPSS) was used for data analysis (IBM Corp., 2017). With Version 25.0, IBM Corp. of Armonk, New York, released IBM SPSS Statistics for Windows. Quantitative and qualitative data were characterised by percentages and counts. To ensure the distribution was normal, the Shapiro-Wilk test was used. Range (including minimum and maximum), mean, standard deviation, median, and interquartile range were used to represent quantitative data (IQR). A significance threshold of 5% was used to evaluate the findings.

4. Results

The age range of patients with AMI was 44–66 years, with a mean of 55.85± 5.49 years. The age range of patients with UA was 38–63 years, with a mean of 54.65± 7.79 years. The control group had an average age of 50.90± 8.64 years, with members ranging from 36–69 years. Of the AMI patients, there were 17 men and 3 females, making up 85 percent and 15 percent, respectively. In the UA group, men made up 75% (n=15) and females 25% (n=5), while in the control group, 60% (n=12) and 40% (n=8) of the participants were male. The age distribution and sex distribution of the groups under study did not vary statistically significantly (p value > 0.05). Table (1).

Table (1) Groups’ demographic information.

<table>
<thead>
<tr>
<th>Variable</th>
<th>MI group (A) (N=20)</th>
<th>UA group (B) (N=20)</th>
<th>Control group (C) (N=20)</th>
<th>Test value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>55.85± 5.49</td>
<td>54.65± 7.79</td>
<td>50.90± 8.64</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>Range</td>
<td>44.0 - 66.0</td>
<td>38.0 - 63.0</td>
<td>36.0 - 69.0</td>
<td></td>
<td>0.098</td>
</tr>
</tbody>
</table>

Table (2) Clinical history of the three groups that were investigated.

<table>
<thead>
<tr>
<th>Variable</th>
<th>MI group (A) (N=20)</th>
<th>UA group (B) (N=20)</th>
<th>Control group (C) (N=20)</th>
<th>Test value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Current</td>
<td>Excessive</td>
<td>Non</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50.0%</td>
<td>45.0%</td>
<td>5.0%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DM</td>
<td>Positive</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>85.0%</td>
<td>15.0%</td>
<td>5.0%</td>
<td></td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>HTN</td>
<td>Positive</td>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>80.0%</td>
<td>20.0%</td>
<td>20.0%</td>
<td></td>
<td>P&lt;0.001</td>
</tr>
</tbody>
</table>

An very significant p value is less than 0.01, while a p-value less than 0.05 is also considered significant. SD stands for standard deviation. X2= Chi-Square test
The results are considered significant when the p-value is less than 0.05 and highly significant when the p-value is less than 0.01. The abbreviations F and KW stand for Kruskal-Wallis and Wilcoxon signed rank tests, respectively. A-B=UA-MI, A-C=MI-Control, and B-C=UA-Control. Time of arrival: initial, and time following arrival: twenty-four hours.

Table (4) Mir-1 in the three groups that were investigated.

<table>
<thead>
<tr>
<th>Mir-1</th>
<th>MI group (A)</th>
<th>UA group (B)</th>
<th>Control group (C)</th>
<th>Test value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean± SD</td>
<td>2.26±0.55</td>
<td>1.60±0.53</td>
<td>1.0±0.0</td>
<td>F= 40.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Range</td>
<td>1.23-3.59</td>
<td>0.95-2.69</td>
<td>1.0-1.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Statistical significance is defined as a p-value of less than or equal to 0.05, with a p-value of less than or equal to 0.01 being highly significant. The analysis was conducted using the F-ANOVA test, with A-B=MI-UA, A-C=MI-Control, and B-C=UA-Control.

5.Discussion

Worldwide, coronary artery disease (CAD) accounts for a disproportionate share of all cardiovascular deaths. Disruption of the atherosclerotic plaque and thrombotic blockage of the artery cause acute coronary syndrome (ACS), a subtype of coronary artery disease (CAD) [1]. Cardiovascular disease (CVD) is one of the diseases that may be detected non-invasively by measuring miRNAs in the blood and other bodily fluids [14]. The non-invasive potential of circulating miRNAs as indicators of cardiovascular diseases such as unstable angina, ST-elevation myocardial infarction (NSTEMI), unstable coronary artery disease (CAD), and acute coronary syndrome (ACS) is now attracting a lot of attention [15]. Potential biomarker possibilities include miRNAs in circulation because of their resistance to ribonuclease and stability across extreme temperatures [15].

Ultimately, miR-1 enhances myoblast development by targeting the production of heat shock proteins (HSP)-60, HSP-70, and Bcl-2. Cardiomyocytes and skeletal muscle produce a lot of it, and it is released into the bloodstream when the heart becomes injured (Lee et al., 2021). Its promise for quick diagnosis is supported by the fact that its level rises in plasma samples taken from patients less than 2 hours after the start of symptoms [13].

The mean age of AMI patients in this study was 55.85±5.49 years, the mean age of UA patients was 54.65±7.79 years, and the mean age of the control group was 50.90±8.64 years. The age range of the AMI patients was 44–66 years, the UA patients were 38–63 years, and the control group was 36–69 years old.

According to research, the average age of patients with acute myocardial infarction was 53.50±10.56 years, whereas the control group had an average age of 52.5±13.50 years [7].

The average age of patients with acute myocardial infarction (AMI) was 59.1±9.2, that of patients with unspecified adverse cardiac events (UA) was 60.4±7.2, and that of the control group was 56.0±8.5, according to further research [16].

According to [17], the average age of patients with acute myocardial infarction was 55.65±11.36, while the non-MI group (including the UA group and the healthy control group) had an average age of 56.86±12.15. These findings were also in agreement with those.

When looking at the age distribution and sex distribution of the groups tested, the present research found no statistically significant difference (p value >0.05).

This was in line with the findings of [18], which showed that the control group and those with acute myocardial infarction did not vary significantly with respect to gender or mean age.

There were no statistically significant variations in age or sex between the UA and control groups, according to another research [19]. Results showed that the groups were significantly different with respect to smoking, diabetes, and hypertension.

Consistent with the current findings, [20] found that there were substantial differences in smoking, hypertension, and DM between the AMI group and the non-AMI groups (UA group and healthy control group).

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According to the results of this investigation, cTnI levels were significantly higher in group A (AMI) compared to group B (UA). This matched the results of a previous research that found an elevated cTnI (p < 0.05) in individuals with AMI compared to those with UA [17]. In terms of cTnI levels, the present investigation showed that group A (AMI) had a much higher rise than group C (control group) (p<0.001).

This jibes with a new research that found cTnI to be higher (p < 0.05) in the AMI group compared to the control group [17].

When comparing the cTnI levels of groups B (UA) and C (control group), no statistically significant difference was found.

There was no statistically significant difference in cTnI between the control group and the UA group, as described in [21].

The results showed that between groups A (AMI) and B, there was a significantly higher level of Mir-1 expression (p<0.001) (UA).

Consistent with previous research, our investigation found that circulating miR-1 levels were much greater in patients with early AMI compared to UA.

The results showed that groups A (AMI) and C had a significantly higher level of early Mir-1 expression (p<0.001) (control group).

In agreement with the current findings, [22] found that miR-1 levels were much greater in AMI patients upon admission compared to healthy controls.

Conclusion

From previous discussion we concluded that miR-1 can be used as early diagnostic marker in patients with acute anterior myocardial infarction (MI) and unstable angina (UA), and could be used as differentiating tool between acute anterior myocardial infarction (MI) and unstable angina (UA).

References


