کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله
Association between Diabetic Retinopathy and Left Ventricular Dysfunction in Diabetic Patients with Unstable Angina

Ebadollah Heidari1, Sanaz Nematzadeh Pakde2, Jahanbakhsh Samadikhah2, Rasoul Azarfarin2, Kamran Shadvar2*

1Department of Ophthalmology, Nikookari Hospital, Tabriz University of Medical Sciences, Tabriz, Iran
2Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz, Iran

Introduc**ton: Diabetes mellitus (DM) is associated with serious complications including macro- and microvascular problems such as diabetic retinopathy. Coronary involvement in diabetic patients is believed to be a consequence of microvascular complications. However, the available data are inconclusive and scarce. This study aimed to evaluate the probable association between diabetic retinopathy and left ventricular dysfunction in diabetic patients with unstable angina (UA).

**Methods:** In this cross-sectional study, 200 diabetic patients with UA (100 cases with diabetic retinopathy and 100 cases without diabetic retinopathy) were enrolled in a teaching hospital. Left ventricular ejection fraction (LVEF) as well as the frequency of cases with left ventricular dysfunction (LVEF<50%) were compared between the two groups and different degrees of diabetic retinopathy (proliferative and non-proliferative).

**Results:** Patients’ demographic variables were comparable between the two groups. Mean diagnosis time of DM was significantly higher in the patients with diabetic retinopathy (8.40±6.60 vs. 3.81±3.58 years; P<0.001). Mean LVEF was significantly lower in the retinopathy group (50.50±6.91% vs. 53.07±4.87%; P=0.003). Frequency of cases with left ventricular dysfunction was significantly higher in the group with diabetic retinopathy (31% vs. 12%; P=0.001, OR=3.33, 95%CI: 1.58-7.14). The frequency of cases with left ventricular dysfunction was significantly yet independently higher in patients with proliferative vs. non-proliferative diabetic retinopathy.

**Conclusion:** Left ventricular dysfunction is more common in diabetic patients with unstable angina and diabetic retinopathy compared with their counterparts without diabetic retinopathy.
and obtaining informed consent from all patients, 200 consecutive patients with unstable angina referred to Madani Heart Hospital were enrolled to investigate the presence of diabetic retinopathy and its relation with left ventricular dysfunction. Inclusion criteria were: 1) Type 2 diabetes mellitus patients with unstable angina; 2) Age of 40 years and older and 3) Willingness to participate in the study.

Exclusion criteria were: 1) Patients with a history of valvular heart disease; 2) A history of myocardial infarction; 3) Patients with cardiomyopathy and congenital heart disease; 4) Patients with chronic heart arrhythmias and 5) Patients with bundle branch block in ECG.

Patients were divided into two groups: 100 patients with retinopathy (case group) and 100 patients without retinopathy (control group). Case group, based on the grading & severity of retinopathy, was divided into four subgroups: Non-proliferative with mild, moderate and severe retinopathy and proliferative groups.

Retinopathy detection was made by an ophthalmologist and retina specialist who were unaware of the status of left ventricular function. Left ventricular function was assessed by a cardiology resident under attending supervision. It should be noted that these two individuals were also unaware of the patient's retinopathy status. In this study, left ventricular dysfunction was defined as LVEF<50%.

Age, sex, weight, height, body mass index (BMI), duration of diabetes mellitus, history of hypertension, history of alcohol consumption, dyslipidemia, left ventricular ejection fraction, ventricular dysfunction and smoking, family history of heart disease and type and severity of diabetic retinopathy were studied.

The obtained information is presented as the mean ± SD, frequency and percentage. SPSS statistical program version 15 was used. Quantitative variables were compared using Student T-test (Independent Samples). Qualitative variables (Categorical) were compared by Contingency tables using Chi-Squared test or Fisher's exact test. \( P \leq 0.05 \) was considered statistically significant.

**Results**

The average age (range) of patients in case group was 59.46 ± 9.06 (38-85) years and 59.08 ± 10.18 (42-79) years in the control group. There was no significant difference between two groups regarding patients’ age \( (P=0.79; \text{Figure 1}) \).

In two groups, demographic characteristics, BMI, hypertension, dyslipidemia, smoking and family history of heart disease were not significantly different (Figure 2). The average duration of diabetes mellitus was significantly higher in case group \( (P<0.001; \text{Figure 3}) \).

None of the patients had a history of alcohol consumption (Figure 4).

Mean LVEF in case group \( (50.50\pm 6.91\%) \) was significantly lower than the control group \( (53.07\pm 4.87\%, P=0.003; \text{Figure 5}) \).

In case and control groups, 31 and 12 patients had left ventricular dysfunction respectively. Percentage of impaired left ventricular function was significantly higher in patients with retinopathy \( (P=0.001; \text{Figure 6}) \).

**Study variables by type of diabetic retinopathy**

Comparison between proliferative and non proliferative (Figure 7): Mean age, sex, and duration of diagnosed diabetes mellitus, hypertension and smoking history, and
family history of heart disease in the two groups were not statistically significant. Percentage of non-proliferative cases with a history of dyslipidemia group was significantly greater. The mean LVEF in proliferative group was significantly low. Percentage of impaired left ventricular function was significantly greater in the proliferative group.

Figure 4. Risk factors percentage in the patients with (case) and without (control) diabetic retinopathy

Figure 5. Left ventricular ejection fraction in the patients with (case) and without (control) diabetic retinopathy

Figure 6. Left ventricular dysfunction in the patients with (case) and without (control) diabetic retinopathy

Comparison between Proliferative and non-Proliferative with different degrees of severity (Table 1): The average duration of diagnosed diabetes mellitus was significantly more in the proliferative group than the mild non-Proliferative groups. Percentage of cases with a history of hypertension was significantly higher in severe non-Proliferative group than other groups. Percentage of cases with a history of dyslipidemia in the proliferative group was significantly less than other groups. Comparing the frequency of cases with smoking history was not possible. The mean LVEF in the proliferative group was significantly less than severe non-proliferative groups. Percentage of impaired left ventricular function in 4 groups showed no significant difference. In other cases, there was no statistically significant difference.

Discussion

In this study, the relationship between diabetic retinopathy and left ventricular dysfunction in diabetic patients with unstable angina was evaluated. Accordingly, the mean LVEF in patients with diabetic retinopathy was significantly lower than the group without diabetic retinopathy. The percentage of impaired left ventricular function in patients with diabetic retinopathy was significantly higher. It has previously been shown that the heart disease in people with diabetes mellitus as retinopathy is caused by microvascular dysfunction. In other words, the underlying pathophysiology in coronary artery disease and diabetic retinopathy is the same.

Two decades ago, Framingham Heart Study suggested that retinopathy symptoms may reflect a microangiopathic process in which the myocardium is also involved. This hypothesis was later approved by the future studies. In these studies, retinopathy signs were associated with T-wave changes in ECG, coronary artery stenosis in the angiographic and histologic evidence of myocardial microvascular disease.

Recent studies using photographic retinopathy grading have introduced stronger evidence on the relationship between retinopathy and cardiac dysfunction. It has been
recognized that the diabetic retinopathy increases the risk of myocardial infarction, coronary artery disease and heart failure.

In a study, Frati et al. evaluated the diabetic patients without cardiovascular symptoms. This study demonstrated that left ventricular dysfunction has a significant relation with duration of diabetes and microvascular disease including diabetic retinopathy. In Fuller and colleagues study, 1126 patients with type 1 diabetes and 3179 patients with type 2 diabetes were studied. After 12 years, diabetic retinopathy increased the risk of heart disease to 1.5 to 2 times in patients with type 2 diabetes. The increased risk was also observed in women with type 1 diabetes while in men with type 1 diabetes, the risk of heart disease was more than 2 times.

Annonu et al. studied 66 type 1 diabetes patients without cardiovascular diseases. This study demonstrated that left ventricular dysfunction is associated with the duration of diabetes and microvascular disease including diabetic retinopathy. Twenty years later, a significant relationship between severity of retinopathy and heart disease was reported.

Wong and colleagues, in a similar study, studied 627 patients with type 2 diabetes. After 7 years, the risk of heart failure in people with retinopathy was more than 2 times those without retinopathy. Juntunnen and colleagues studied 824 patients with type 2 diabetes. After 18 years, proliferative retinopathy increased the risk of heart disease more than 2 times in these individuals compared to the controls. Only in women Non-proliferative retinopathy was reported as a risk factor for heart disease.

Cheung and colleagues studied 1021 middle-aged patients with type2 diabetes with normal renal function and no symptoms of coronary artery disease and heart failure. Retinopathy severity and the incidence of heart failure and mortality associated with the severity of retinopathy were evaluated. Some (12.8%) of these patients had diabetic retinopathy. After 9 years, 10.1% of the patients developed heart failure. The incidence of heart failure in people with retinopathy was significantly higher (cumulative incidence of 6.12% vs. 5.8%). After controlling other risk factors, diabetic retinopathy increased the risk of heart failure by 2.5 times.

Mishra and colleagues studied 73 diabetic patients without symptoms of heart disease. Echocardiographic systolic and diastolic function was assessed separately. Finally, it was shown that there was significantly higher number of diabetic retinopathy cases in patients with left ventricular dysfunction. Additionally, this status was significantly associated with duration of diabetes mellitus. Aguilar and colleagues studied 531 patients with type 2 diabetes. In this study it was demonstrated that increase in these severity of retinopathy increased left ventricular mass and left atrial dimension and LVEF, independent of confounding variables, decreased.

As can be seen, our results are in line with existing reports. In our study, significant association was present between diabetic retinopathy and duration of diabetes mellitus; left ventricular dysfunction independent of this parameter was significantly higher in the group with diabetic retinopathy. To the best of our knowledge, no similar study on patients with unstable angina has been conducted so far. In this study, the correlation between left ventricular dysfunction and the type and severity of diabetic retinopathy was studied. Accordingly, the percentage of impaired left ventricular function in patients with proliferative diabetic retinopathy was significantly higher than non-proliferative cases. However, after controlling for confounding factors, this significance disappeared.

Van Hecke et al. in their study on 2237 patients with type 1 diabetes mellitus showed that mortality from cardiovascular events in proliferative diabetic retinopathy is about 4 times higher than patients suffering from non-proliferative diabetic retinopathy. However, this relationship became insignificant after controlling for

### Table 1. Variables were compared according to the type and severity of diabetic retinopathy

<table>
<thead>
<tr>
<th>Age (year)</th>
<th>Total (n=60)</th>
<th>Mild (n=44)</th>
<th>Mod (n=20)</th>
<th>Sever (n=16)</th>
<th>P*</th>
<th>P**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration Of Diabetes(year)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>7.84± 5.97</td>
<td>6.16± 4.21</td>
<td>9.35± 7.15</td>
<td>10.73± 7.31</td>
<td>0.08</td>
<td>0.01</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>33.8±17</td>
<td>38.6±17</td>
<td>25±9</td>
<td>31.3±5</td>
<td>0.01</td>
<td>0.04</td>
</tr>
<tr>
<td>Smoke</td>
<td>16.3±13</td>
<td>18.2±13</td>
<td>15±3</td>
<td>12.5±2</td>
<td>0.11</td>
<td>-</td>
</tr>
<tr>
<td>Positive Family History CVD</td>
<td>6.3±1</td>
<td>4.5±1</td>
<td>15±3</td>
<td>0±1</td>
<td>0.65</td>
<td>-</td>
</tr>
<tr>
<td>LVEF(%)</td>
<td>51.3± 5.99</td>
<td>50.2± 5.90</td>
<td>52.0± 6.77</td>
<td>53.4± 6.73</td>
<td>0.01</td>
<td>0.03</td>
</tr>
<tr>
<td>LV. Dysfunction</td>
<td>26.3±21</td>
<td>31.8±14</td>
<td>25±5</td>
<td>12.5±2</td>
<td>0.04</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Data are demonstrated as mean±SD or number (%), BMI: Body mass index, LVEF: Left ventricular ejection fraction, CVD: Cardio vascular diseases, LV: Left ventricle, *Proliferative vs. Non proliferative, **Proliferative vs. severities of Non proliferative
other risk factors for cardiovascular disease.\textsuperscript{21} Reaven and colleagues showed that coronary calcium has a direct relationship with diabetic retinopathy. This relationship in patients with proliferative diabetic retinopathy was significantly higher than patients with non-proliferative diabetic retinopathy.\textsuperscript{22}

As can be seen, the results of our study are in line with previous reports in this field. However, to evaluate more carefully, further studies with larger sample size are required.

**Conclusion**

In our study, 31\% of diabetic patients with retinopathy and unstable angina had left ventricular dysfunction. While, in diabetic patients without retinopathy and with unstable angina, left ventricular dysfunction was seen in only 12\% of cases. Percentage of impaired left ventricular function in patients with unstable angina and a sign of retinopathy are significantly higher than the group without retinopathy. There was no association between left ventricular dysfunction, type, and severity of diabetic retinopathy in patients with unstable angina. Although the risk of left ventricular dysfunction in patients with proliferative diabetic retinopathy is more than non-proliferative, in order to reach conclusive results, further studies with larger sample size are recommended.

**Acknowledgment**

This research project was funded by Cardiovascular Research Center, Tabriz University of Medical Sciences.

**Conflict of interests:** The authors declare no conflicts of interest.

**References**

کارگاه‌های آموزشی مرکز اطلاعات علمی

مقاله نویسی علوم انسانی

اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله