

# CLUSTERING OF CARDIOVASCULAR RISK FACTORS IN DIABETICS AND IGT CASES IN ISFAHAN PROVINCE 2000-2001: ISFAHAN HEALTHY HEART PROGRAM

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## Abstract

**INTRODUCTION:** This study was conducted to cluster cardiac risk factors of patients and to compare the prevalence of these risk factors in diabetic patients and patients with glucose intolerance with normal people, and also to compare the prevalence of these factors in known and new cases of diabetes mellitus.

**METHODS:** This descriptive cross-sectional study was conducted on a sample selected from Isfahan province, Iran, as part of a national program for cardiovascular diseases prevention and control. A total of 3940 male and female subjects (1914 males, 2026 females) aged above 19 years were studied. The demographic characteristics were obtained by questionnaire. Important risk factors such as Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Waist Circumference (WC), Body Mass Index (BMI), Fasting Blood Sugar (FBS), Triglyceride (TG), Total Cholesterol (TC), High Density Lipoprotein (HDL-C), and Low Density Lipoprotein (LDL-C) were assessed in the subjects.

**RESULTS:** The prevalence of known cases of diabetes, new cases of diabetes, and glucose resistance was 4.3%, 1.1%, and 6.2% in the population under study, respectively. The prevalence of the above conditions was 4.9%, 1.2% and 1.1% in women, and 3.7%, 1% and 5.3% in men, respectively. Comparison of the prevalence of blood lipid disorders showed a significant difference between patients and healthy individuals. The overall comparison of all of the risk factors also showed a significant difference between the said groups. The prevalence of blood lipid disorders in men was higher than in women and this difference was significant. Comparison of the prevalence of increased BMI/WC and blood lipid disorders between two sexes revealed a significantly higher prevalence in women.

**DISCUSSION:** The results of this study indicate a high prevalence of risk factors, especially increased prevalence of obesity and blood lipid disorders in cases of diabetes and glucose intolerance. Hence, strategies for prevention and treatment of diabetes should be launched in the community in view of the extent of these risk factors.

**Keywords** ● Clustering of risk factors ● Known cases of diabetes ● New cases of diabetes  
● Glucose intolerance

**ARYA Journal, 2005, 1(2): 94-100**

## Introduction

Diabetes is an important cause of death worldwide. There are more than 154 million diabetics throughout the world.<sup>1</sup> The costs of treating diabetes reach 98 million dollars in the United States annually.<sup>2,3</sup> The prevalence of diabetes is on the rise in developing countries.<sup>4</sup>

Epidemiological studies on diabetes in Iran have estimated the prevalence of diabetes at 10.6% in the over-30 population.<sup>4</sup> Several underlying factors are involved in the etiology of type II diabetes. Impaired Glucose Tolerance (IGT) and obesity are among important diabetes risk factors.<sup>5</sup> Epidemiological studies conducted by Framingham show that diabetics have a 2-4 times higher risk of developing cardiovascular diseases including myocardial infarction.<sup>6,7</sup> Increased risk of cardiovascular diseases in diabetics is accompanied by lipid and lipoprotein metabolism disorders.<sup>7,8</sup> Various studies have shown the prevalence of hypertension in diabetics may be

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twice as high as normal individuals.<sup>9,10</sup> Results of WHO-ERICA and Framingham studies have clearly highlighted the importance of classifying the risk factors.<sup>11,12</sup> This study was carried out to compare individuals with diabetes/impaired glucose tolerance test and known and new cases of diabetes in respect of the prevalence of some cardiovascular risk factors.

### Materials and methods

This is a descriptive cross-sectional studies based on data obtained from phase I of Isfahan Healthy Heart Program (IHHP) in 2000-2002. Sampling was conducted using the systematic method (randomized cluster).<sup>13</sup> 3940 individuals were studied. Being aged above 19 years, absence of hemorrhagic diseases and mental retardation, Iranian nationality, and having lived in Isfahan for at least six months comprised the criteria of inclusion in the study. Subjects who did not meet these criteria and pregnant women were excluded. Given the equal distribution of the two sexes in the Iranian population, equal numbers of men and women were selected for the study.

The validity and reliability of the questionnaire used to collect data was twice verified in two experimental stages.<sup>13</sup> Height and weight of subjects were measured while the subjects did not wear shoes and had light clothing. German-made Secca® scales were used and measurements were conducted by trained individuals. Waist Circumference (WC) was also measured in standing position and with light clothing. Body Mass Index (BMI) was measured using the formula:<sup>14</sup>

$$\frac{\text{weight(kg)}}{\text{Height}^2(\text{m})}$$

Subjects with  $25 \leq \text{BMI} \leq 29.9$  and  $30 \leq \text{BMI}$  were considered as overweight and obese, respectively.<sup>15</sup>  $\text{WC} \geq 88$  cm in women, and  $\text{WC} \leq 102$  cm in men was considered as a risk factor.<sup>16</sup> Blood pressure (BP) was measured by trained physicians according to standard criteria, using mercury sphygmomanometers. Blood pressure was measured twice on right hand after 5 minutes of rest and the average of the two readings was recorded as the subject's blood pressure. Based on WHO definition, individuals with systolic  $\text{BP} \geq 140$  mmHg or diastolic  $\text{BP} \geq 90$  mmHg were considered as hypertensive.<sup>15</sup> Blood samples were taken from the subjects after 14 hours in fasting state. Biochemical tests, including measurement of total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) were carried out. TC and TG were measured by German made Ependrof Elan 2000 autoanalyzer using the enzymatic method.

HDL-C was measured using heparin-manganese precipitation method.<sup>18</sup>

LDL cholesterol (LDL-C) was measured in samples containing  $\leq 400$  mg/dl TG using Friedwald formula.<sup>19</sup> It was otherwise measured using a special test kit. Subjects with  $\text{TG} \geq 200$ ,  $\text{TC} \geq 240$ ,  $\text{HDL-C} \leq 40$ , or  $\text{LDL} > 100$  (mg/dl) were considered as dyslipidemic.<sup>20</sup> Sodium fluoride was used to isolate plasma from samples before measuring blood sugar. Blood sugar was measured using glucose oxidase enzymatic method. All laboratory procedures were carried out at the laboratory of Isfahan Cardiovascular Research Center (ICRC). This laboratory meets criteria of Iran Health Ministry and is qualitatively controlled by the University of Stafaello in Brussels, Belgium. In this study subjects with fasting blood sugar (FBS)<sup>2</sup>  $\geq 126$  mg/dl or those on anti-diabetic medications were considered as being diabetic.<sup>21</sup> Known diabetics were defined as those whose diabetes mellitus had been earlier established by a physician or those who received anti-diabetic medications. IGT<sup>3</sup> criteria is based on 2-hour postprandial blood glucose level, i.e.  $140 \leq 2\text{hpp}^4 \leq 200$ .<sup>21</sup>

#### Data analysis

The frequency of cardiovascular risk factors including hypertension, increased WC, increased BMI and disorders of lipid profiles were compared independently of each other, in the groups under study, i.e. known and new cases of diabetics, cases of IGT and normal individuals. The combined effects of these risk factors were also compared in the population under study. The frequency distribution of the risk factors was compared between the two sexes, as well as between known and new cases of diabetes and normal individuals with chi-square and Fisher Exact tests using SPSS11/win software.

### Results

A total of 3940 subjects including 2020 women and 1919 men were studied. Women and men had mean ages of  $38.7 \pm 0.31$  and  $39 \pm 0.35$  years, respectively. Mean fasting blood glucose level was  $85.4 \pm 0.57$  and mean 2-hour blood glucose level was  $104.9 \pm 0.91$  mg/dl. Mean body mass index and mean waist circumference measured  $26.2 \pm 0.09$  and  $94.1 \pm 0.2$  cm, respectively. The prevalence of known cases of diabetes, new cases of diabetes and cases of IGT was 4.3%, 1.1%, and 6.2%, respectively. The prevalence of known cases of diabetes, new cases of diabetes and cases of IGT was 4.9%, 1.2%, and 7.1% respectively in women, and 3.7%, 1%, and 5.3% respectively in men.

**TABLE 1.** Comparison of the frequency of cardiovascular risk factors between new/known cases of diabetes/cases of IGT and normal individuals according to sex

|  | Men   |              |           |       |              |                               | Women |              |           |      |              |                             |       |              |                               |
|--|-------|--------------|-----------|-------|--------------|-------------------------------|-------|--------------|-----------|------|--------------|-----------------------------|-------|--------------|-------------------------------|
|  | P     | Normal N (%) | IGT N (%) | P     | Normal N (%) | Known cases of diabetes N (%) | P     | Normal N (%) | IGT N (%) | P    | Normal N (%) | New cases of diabetes N (%) | P     | Normal N (%) | Known cases of diabetes N (%) |
| Hypertension*                                  | 0.9   | 11(6)        | 0         | 0.9   | 11(6)        | 1(1.3)                        | 0.3   | 11(6)        | 4(2)      | 0.9  | 4(2)         | 0                           | 0.9   | 4(2)         | 0                             |
| Overweight**                                   | 0.3   | 58(3)        | 1(1)      | 0.9   | 58(3)        | 0                             | 0.1   | 58(3)        | 79(4)     | 0.9  | 79(4)        | 0                           | 0.7   | 79(4)        | 3(2.8)                        |
| Obesity***                                     | 0.6   | 18(1)        | 0         | 0.9   | 18(1)        | 1(1.4)                        | 0.5   | 18(1)        | 46(2.3)   | 0.4  | 46(2.3)      | 1(4)                        | 0.1   | 46(2.3)      | 0                             |
| Increased waist circumference*                 | 0.6   | 19(1)        | 0         | 0.9   | 19(1)        | 1(1.4)                        | 0.04  | 172(8.8)     | 6(4)      | 0.7  | 172(8.8)     | 1(4.3)                      | 0.03  | 172(8.8)     | 3(2.8)                        |
| Lipid disorders**                              | 0.001 | 630(34)      | 15(15)    | 0.001 | 630(34)      | 12(14)                        | 0     | 630(34)      | 3(2)      | 0.06 | 241(12)      | 0                           | 0.001 | 241(12)      | 1(1)                          |
| Hypertension + increased BMI                   | 0.4   | 11(6)        | 1(1)      | 0.1   | 11(6)        | 1(4.8)                        | 0.4   | 11(6)        | 18(9)     | 0.9  | 18(9)        | 0                           | 0.9   | 18(9)        | 0                             |
| Hypertension + increased WC                    | 0.9   | 3(2)         | 0         | 0.9   | 3(2)         | 0                             | 0.9   | 3(2)         | 23(1.2)   | 0.9  | 23(1.2)      | 0                           | 0.6   | 23(1.2)      | 0                             |
| Hypertension + lipid disorders                 | 0.06  | 68(3.7)      | 8(8)      | 0.5   | 68(3.7)      | 10(13)                        | 0.001 | 68(3.7)      | 42(7)     | 0.2  | 23(1.2)      | 1(4)                        | 0.6   | 23(1.2)      | 0                             |
| Increased BMI + lipid disorders                | 0.09  | 583(32)      | 41(39)    | 0.1   | 583(32)      | 25(34)                        | 0.6   | 583(32)      | 82(55)    | 0.2  | 778(40)      | 12(52)                      | 0.07  | 778(40)      | 34(32)                        |
| Increased WC + lipid disorders                 | 0.001 | 169(9)       | 23(22)    | 0.01  | 169(9)       | 6(29)                         | 0.3   | 169(9)       | 923(47)   | 0.7  | 923(47)      | 12(52)                      | 0.1   | 923(47)      | 43(41)                        |
| Hypertension + increased BMI + lipid disorders | 0.001 | 156(9)       | 29(26)    | 0.001 | 156(9)       | 8(38)                         | 0.001 | 156(9)       | 37(24.8)  | 0.03 | 220(12)      | 6(27)                       | 0.001 | 220(12)      | 45(44)                        |
| Hypertension + increased WC + lipid disorders  | 0.001 | 99(6)        | 19(19)    | 0.001 | 99(6)        | 6(29)                         | 0.001 | 99(6)        | 42(28.2)  | 0.01 | 243(13)      | 7(32)                       | 0.001 | 243(13)      | 52(50)                        |

♣ Blood glucose level 2 hours after glucose intake < 140 mg/dl or receiving no glucose-lowering medications

\* Hypertension: systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or receiving glucose-lowering medication(s)

\*\* 30 > BMI ≥ 25

\*\*\* BMI ≥ 30

● Increased WC: > 88 cm in women, > 102 cm in men,

●● Lipid disorders: triglyceride (TG) ≥ 200, HDL-c < 40 mg/dl, total cholesterol (TC) ≥ 240 mg/dl, LDL-c > 100 mg/dl

**TABLE 2.** Comparison of the frequency of some cardiovascular risk factors in known and new cases of diabetes according to sex

|  | Women                      |                              | Men                        |                              | P    | Total                      |                              |
|--|----------------------------|------------------------------|----------------------------|------------------------------|------|----------------------------|------------------------------|
|  | New cases of diabetes (N%) | Known cases of diabetes (N%) | New cases of diabetes (n%) | Known cases of diabetes (N%) |      | New cases of diabetes (N%) | Known cases of diabetes (N%) |
| Hypertension*                                  | -                          | 0                            | 0                          | 1(1.3)                       | 0.9  | 0                          | 1(6)                         |
| Overweight**                                   | 0.9                        | 0                            | 0                          | 0                            | 0.9  | 0                          | 3(1.7)                       |
| Obesity***                                     | 0.1                        | 1(4)                         | 0                          | 1(1.4)                       | 0.3  | 1(2.2)                     | 1(6)                         |
| Increased waist circumference*                 | 0.5                        | 1(4.3)                       | 0                          | 1(1.4)                       | 0.9  | 1(2.3)                     | 4(2.2)                       |
| Lipid disorders**                              | 0.5                        | 1(4.3)                       | 0                          | 1(1.4)                       | 0.07 | 0                          | 13(7.3)                      |
| Hypertension + increased BMI                   | -                          | 0                            | 0                          | 0                            | 0.2  | 1(2.2)                     | 0                            |
| Hypertension + increased WC                    | -                          | 0                            | 0                          | 0                            | -    | 0                          | 0                            |
| Hypertension + lipid disorders                 | -                          | 1(4)                         | 0                          | 1(4.8)                       | 0.4  | 1(4.3)                     | 10(5.5)                      |
| Increased BMI + lipid disorders                | 0.06                       | 12(52.2)                     | 34(32.1)                   | 25(34.2)                     | 0.03 | 22(50)                     | 59(33)                       |
| Increased WC + lipid disorders                 | 0.3                        | 12(52.2)                     | 43(40.6)                   | 9(12.3)                      | 0.1  | 18(40.9)                   | 52(29.1)                     |
| Hypertension + increased BMI + lipid disorders | 0.1                        | 6(27.3)                      | 45(43.7)                   | 20(27.8)                     | 0.5  | 14(32.6)                   | 65(37.1)                     |
| Hypertension + increased WC + lipid disorders  | 0.1                        | 7(31.8)                      | 52(50)                     | 13(18.1)                     | 0.4  | 13(30.2)                   | 65(36.9)                     |

\* Blood glucose level 2 hours after glucose intake < 140 mg/dl or receiving no glucose-lowering medications, \* Hypertension: systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or receiving glucose-lowering medication(s), \*\* 30 > BMI ≥ 25, \*\*\* BMI ≥ 30, • Increased WC: > 88 cm in women, > 102 cm in men, •• Lipid disorders: triglyceride (TG) ≥ 200, HDL-c < 40 mg/dl, total cholesterol (TC) ≥ 240 mg/dl, LDL-c > 100 mg/dl

**TABLE 3.** Comparison of the frequency of some cardiovascular risk factors between men and women, in known/new cases of diabetes/glucose intolerance

|  | IGT    |             |           |     | New cases of diabetes |           |        |             | Known cases of diabetes |        |             |           |
|--|--------|-------------|-----------|-----|-----------------------|-----------|--------|-------------|-------------------------|--------|-------------|-----------|
|  | P      | Women N (%) | Men N (%) | P   | Women N (%)           | Men N (%) | P1     | Women N (%) | Men N (%)               | P1     | Women N (%) | Men N (%) |
| Hypertension*                                  | 0.9    | 1(7)        | 0         | -   | 0                     | 0         | 0.4    | 0           | 1(1.3)                  | 0      | 0           | 1(1.3)    |
| Overweight**                                   | 0.07   | 4(2.7)      | 1(1)      | -   | 0                     | 0         | 0.2    | 3(2.8)      | 0                       | 0.2    | 3(2.8)      | 0         |
| Obesity***                                     | 0.6    | 2(1.3)      | 0         | 0.9 | 1(4)                  | 0         | 0.4    | 0           | 1(1.4)                  | 0.4    | 0           | 1(1.4)    |
| Increased waist circumference*                 | 0.6    | 6(4)        | 0         | 0.9 | 1(4.3)                | 0         | 0.6    | 3(2.8)      | 1(1.4)                  | 0.6    | 3(2.8)      | 1(1.4)    |
| Lipid disorders**                              | <0.001 | 3(2)        | 15(14.6)  | -   | 0                     | 0         | <0.001 | 1(1)        | 12(16.2)                | <0.001 | 1(1)        | 12(16.2)  |
| Hypertension + increased BMI                   | 0.6    | 1(0.7)      | 1(1)      | 0.4 | 0                     | 1(4.8)    | -      | 0           | 0                       | -      | 0           | 0         |
| Hypertension + increased WC                    | 0.5    | 1(0.7)      | -         | -   | 0                     | 0         | -      | 0           | 0                       | -      | 0           | 0         |
| Hypertension + lipid disorders                 | 0.07   | 4(2.7)      | 8(7.6)    | 0.7 | 1(4)                  | 1(4.8)    | <0.001 | 0           | 10(13.3)                | <0.001 | 0           | 10(13.3)  |
| Increased BMI + lipid disorders                | 0.1    | 73(49)      | 41(39)    | 0.7 | 12(52)                | 10(48)    | 0.7    | 34(32)      | 25(34)                  | 0.7    | 43(41)      | 9(12)     |
| Increased WC + lipid disorders                 | 0      | 82(55)      | 23(22.1)  | 0.1 | 12(52.2)              | 6(28.6)   | <0.001 | 43(41)      | 20(28)                  | <0.001 | 45(44)      | 20(28)    |
| Hypertension + increased BMI + lipid disorders | 0.5    | 37(25)      | 29(28)    | 0.4 | 6(27)                 | 8(38)     | 0.03   | 45(44)      | 20(28)                  | 0.03   | 45(44)      | 20(28)    |
| Hypertension + increased WC + lipid disorders  | 0.08   | 42(28)      | 19(19)    | 0.8 | 7(32)                 | 6(29)     | <0.001 | 52(50)      | 13(18)                  | <0.001 | 52(50)      | 13(18)    |

Table 1 shows the results of comparing the frequencies of some of the cardiac risk factors in known cases of diabetes, new cases of diabetes and cases of IGT in the two sexes. In both sexes, comparison of the frequency of the combination of risk factors between known/new cases of diabetes/cases of IGT and normal individuals showed a significant difference ( $P < 0.05$ ).

Table 2 compares the frequency of risk factors individually/collectively between known/new cases of diabetes in both sexes.

Except for the combination of increased BMI and lipid profile, assessment of other risk factors, alone or in combination with each other, in known/new cases of diabetes did not show a significant difference ( $P > 0.05$ ).

Table 3 compares the frequency of cardiac risk factors between the two sexes in known/new cases of diabetes and cases of IGT, showing that the prevalence of lipid disorders alone is significant according to sex ( $P < 0.05$ ).

Comparison of the frequency of the combination of lipid disorders and hypertension in cases of known diabetes, as well as the combination of lipid profile disorders and increased waist circumference in cases of known diabetes and IGT revealed a significant difference ( $P < 0.05$ ).

Comparison of the combination of risk factors between men and women revealed a significant difference only in known cases of diabetes ( $P < 0.05$ ).

## Discussion

Several studies have documented the increasing prevalence of non-communicable diseases including diabetes and its associated complications.<sup>22,23</sup> In this study, the prevalence of new cases of diabetes was significantly lower than that of known cases of diabetes.

Studies in the US, Sudan, Iraq, and Kuwait have shown the prevalence of new and known cases of diabetes to be equal.<sup>24,25</sup>

Identification of new cases of diabetes could be effective in management of the disease, prevention of its micro- and macrovascular complications, and blood sugar control.<sup>26</sup> An Iranian study found a higher prevalence of diabetes in the population of women as compared to men, which is partly due to greater female predisposition to the disease. The difference in lifestyle is more obvious in women. Immobility, obesity and unhealthy diet were seen more frequently in women.<sup>27,28</sup> The prevalence of IGT in the general population is about 6.2%. Prospective studies have shown that ??% of individuals with IGT are at risk of developing

diabetes.<sup>29</sup> Several factors are involved in increasing the risk of atherosclerosis in diabetic patients. These factors include increased blood glucose and resistance to insulin.

Resistance to insulin could be considered as an isolated risk factor or in combination with other risk factors.<sup>30,31</sup> Table 1 compares the frequency of risk factors between normal individuals and known/new cases of diabetes/cases of IGT.

When the prevalence of cardiac risk factors was compared independently between the two groups, a significant difference was seen in both sexes only for two risk factors, namely increased waist circumference and lipid profile disorders. Distribution of central obesity is known as a diabetes risk factor.<sup>32</sup> Other studies have shown that central obesity is a more important indicator in predicting cardiovascular disease and diabetes than BMI. Women are more prone to develop diabetes.<sup>33</sup> Results of studies performed on Indian Americans have shown that there is no relationship between hypertension and increased levels of fasting insulin in the absence of increased blood glucose and lipid disorders. The strongest relationship is observed when lipid profile disorders are considered as a risk factor in hyperglycemic patients.<sup>34,35</sup> Lipid disorders have been recognized as a major mortality risk in diabetic patients.<sup>36</sup> Comparison of the frequency of the combination of several risk factors reveals a significant difference between diabetics and normal individuals in terms of the prevalence of risk factors (Table 1).

In IGT cases, this difference can even be seen in patients with hypertension and lipid profile disorders. Studies conducted by Zimmet and colleagues have shown a strong relationship between increased insulin resistance and IGT.<sup>36</sup> This relationship strengthens in the presence of multiple risk factors,<sup>37</sup> which combine to exert a synergistic effect.<sup>37</sup> Except in cases of increased BMI occurring concomitantly with lipid disorders, comparison of risk factors between new and known cases of diabetes (table 2) revealed no significant difference. Several studies have shown that the prevalence of cardiac risk factors is high in all cases of diabetes, including new ones.<sup>34</sup> This indicates the rapid progression of vascular damages in diabetics and highlights the necessity of enforcing a continuous screening system for identification and control of diabetes. These risk factors are seen frequently, even in patients who are in the early stages of developing IGT.<sup>39</sup>

In this study, comparison of the combination of risk factors between normal individuals and those with IGT showed a significant difference ( $P < 0.05$ ).

Comparison of the prevalence of lipid disorders between men and women shows that lipid disorders alone can be considered as a risk factor in hyperglycemic individuals, especially men (table 3). Studies have shown lipid disorders to be an important risk factor for atherosclerosis in diabetic patients,<sup>41</sup> however, this relationship is stronger in men. This could be due to more rapid increase in total cholesterol (TC) and low-density lipoprotein (LDL-C) in men or the higher concentration of HDL-C in women, since the latter serves to protect against increase in TG and LDL-C.<sup>42</sup>

In the present study, comparison of the frequency of lipid disorders combined with increased obesity indices (increased WC, increased BMI) revealed a higher prevalence of these risk factors in women. This difference is significant in known cases of diabetes. As previously noted, the prevalence of diabetes in women is higher than in men. Several studies including the National Health and Nutrition Examination Survey (NHNES) have shown that the prevalence of overweight and obesity is higher in women, both in cases of diabetes and IGT.<sup>43</sup>

The results of this study demonstrate the high prevalence of risk factors, especially obesity and lipid disorders in the diabetic population of the city of Isfahan. A high frequency of risk factors is seen in all diabetic groups, even new cases of diabetes and cases of IGT. Hence strategies for prevention and management of diabetes should be based on the extent of the risk factors involved.

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