

*Original Article***A novel prediction model for all cause emergency department visits in ischemic heart disease***Bahram Pishgoo<sup>a</sup>***Abstract**

**BACKGROUND:** Ischemic heart disease (IHD) is the main cause of morbidity and mortality worldwide, and a considerable part of these patients attend to emergency departments, which increases the burden to these busy departments. The aim of this study was to develop a prediction model enabling prediction of all cause emergency department (ED) visits in patients with documented coronary stenosis in a derivation set, and then to determine its accuracy in a validation set.

**METHODS:** In a prospective study at outpatient setting of Baqiyatallah hospital, Tehran, Iran, 502 patients with IHD were followed for 6 months for observing the outcome of ED visits for all causes. They were divided in two random groups of derivation set (n = 335) and validation set (n = 167). In the derivation set, to achieve an all cause ED visits prediction model, a prediction model was reached by entering demographic data, clinical variables, somatic comorbidity (Ifudu index), level of anxiety and depression (Hospital Anxiety Depression Scale (HADS) questionnaire), and angina grade (WHO Rose Angina) to a logistic regression. Then in the validation set, the sensitivity, specificity, and the accuracy of that model was tested.

**RESULTS:** A novel model for prediction of all cause ED visits in IHD patients in six months was presented with gender, anxiety, WHO angina grade and somatic comorbidity as inputs. Sensitivity, specificity, and accuracy of the model were 63.0%, 68.6%, and 67.7%, respectively.

**CONCLUSIONS:** Testing and using the achieved model is suggested to health care providers in other settings.

**KEYWORDS:** Emergency Hospital Services, Office Visit, Coronary Artery Disease, Ischemic Heart Disease.

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I schemic heart disease (IHD) is the main cause of mortality worldwide. The number of deaths due to IHD still shows a worldwide increase<sup>1,2</sup> which will render it the leading cause of death till 2020.<sup>3,4</sup> In the US, more than 12 million people suffer from IHD and more than 1 million have experienced an acute myocardial infarction or fatal IHD each year, resulting in over 466,000 annual deaths attributed to IHD.<sup>5</sup>

Most researches in the area of health care used for IHD has focused on in-patient care rather than those in the out-patient settings.<sup>6</sup> However it is known that only in the US, IHD is responsible for 2 to 3 million emergency department (ED) visits.<sup>7</sup> This figure necessitates investigations into probable ED visits by IHD

patients to find modifiable risk factors which put IHD patients at higher risk of ED visits and help healthcare system reduce the associated public health burden.

In the present study, it is tried to develop a model of prediction of all cause ED visits in patients suffering from IHD during six months and test the accuracy of the model on another, yet similar, group of patients.

**Methods***Design and Setting*

This prospective study was conducted as a part of a grant focusing of morbidity of patients with chronic condition in Baqiyatallah hospital, Tehran, Iran, in 2006-2007. Other reports have been published from the study.<sup>8,9</sup>

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### ***Participants and Sampling***

This study was conducted in cardiology outpatient clinic of the Baqiyatallah hospital, Tehran, Iran, in 2006 and 2007. The inclusion criterion was having significant IHD defined as  $\geq 50\%$  stenosis in at least one major coronary artery, confirmed by angiography.

### ***Measures and Measurement***

#### **Baseline Data**

Patients' age, gender, marital status, education level, living place, monthly family income and Body Mass Index (BMI) was registered, in addition to somatic comorbidity, anxiety and depression and angina grade.

#### **Somatic Comorbidity**

Somatic comorbidities were assessed using Ifudu Comorbidity Index. The original Ifudu Comorbidity Index is a numerical self-rated questionnaire that investigates the presence of 13 different chronic somatic illnesses in addition to chronic mental comorbidities, and provides a total score between 0 and 42. Higher Ifudu scores demonstrate having more comorbidity. The somatic conditions which are being assessed include: 1) nonischemic heart disease/hypertension, 2) ischemic heart disease, 3) chronic respiratory disease, 4) visual impairment, 5) low back pain, spine or joint disorders, 6) other musculoskeletal disorders, 7) genitourinary diseases, 8) hematological disease, 9) autonomic neuropathy, 10) infections, 11) liver, pancreas or biliary disease, 12) peripheral vascular disease, and 13) other neurologic disease.<sup>10</sup> As all the present patients had IHD, and their somatic comorbidity was measured, the modified version of Ifudu index was composed of 12 non-IHD somatic comorbidities and ranged from 0 to 36. Although this measure is originally developed for patients with chronic kidney disease, this measure has been repeatedly used in a wide range of other chronic conditions such as respiratory diseases, blood diseases, and rheumatologic conditions.<sup>11-15</sup>

### **Anxiety and Depression**

Anxiety and depression were assessed using a Persian translated and validated version of the Hospital Anxiety Depression Scale (HADS).<sup>16</sup> HADS contains 14 items and yields two subscales: anxiety and depression. Scores for each subscale ranges from 0 to 21, with higher scores indicating more severe symptoms.<sup>17</sup>

#### **Angina Grade**

For this purpose Rose Angina Questionnaire was used as below:<sup>18</sup>

**Angina Grade I:** respondents reported pain that met the criteria for any exertional chest pain and that the pain caused them to stop or slow down, relieved when the respondent stood still, disappeared within 10 minutes or less, occurred in the sternum, left arm and/or left anterior of the chest and did not occur when walking at an ordinary pace on the level.

**Angina grade II:** respondents reported pain that met the criteria for grade I Rose angina, and reported that the pain occurred when walking at an ordinary pace on the level.

#### **All Cause Emergency Department Visit**

Number of all cause emergency department visit during six months follow up period was the main outcome of the study and was defined as "all of the patient's visits to ED physician for any reason" and was asked through monthly phone calls.

#### **Codes of Ethics**

The study was approved by the ethics board of the university and informed consent was obtained from all participants.

#### **Statistical Analysis**

In order to establish an accurate model for predicting the all cause ED visits by patients, firstly participants were randomly divided into two groups: 335 patients formed the "derivation set", based on which the prediction model was set, and the other 167 patients made the "validation set", which the accuracy of the

model was tested upon them. These two groups were not significantly different in baseline characteristics such as age, gender, marital status, family income, educational status, living place, BMI, anxiety, depression, angina type and somatic comorbidity (Chi square and independent sample t-test) (Table 1).

In the next step, a logistic regression model was implemented which predicts the probability of a binomial outcome.

The last step of the analysis was the validation process in which the suggested model was tested on "validation set" population to see whether it can predict the outcome (the probability of all cause ED visit) correctly. Then sensitivity, specificity, and accuracy of the model were calculated.

To know how valid the regression analysis is, sensitivity and specificity curves were plotted for different levels of the probabilities of the estimated model. This was then used to find the model-estimated probability cutoff, at which optimal sensitivity and specificity were achieved, namely maximal sum of sensitivity and specificity point of crossing.<sup>19</sup> Data analysis was performed using SPSS version 13 for windows and p values less than 0.05 were considered statistically significant.

## Results

From the 600 consecutive IHD outpatients who were invited, 550 accepted to enroll, and 502 patients successfully completed the study and entered the current analysis.

### Derivation Set

In the derivation set, 66 (19.7%) patients visited ED, for any cause. Tables 2 and 3 compare the baseline data among patients with and without ED visit in this patient set.

In brief, the model showed that the estimated probability of all cause ED visit in IHD patients was a function of gender, anxiety symptoms, somatic comorbidity score, and presence of grade I or II of chest pain according to Rose angina questionnaire. The summary of regression analysis (in derivation set) is listed in table 4.

According to the logistic regression analysis, the following statistical equation could predict all cause ED visit in IHD patients:

$$\text{Log } P = 0.060 \times \text{anxiety} + 0.060 \times \text{somatic comorbidity} + 0.561 (\text{if male gender}) + 0.689 (\text{if having grade I or II angina}) - 3.501$$

In this equation, P stands for the probability of six month all cause ED visit, anxiety and somatic comorbidity are the scores of anxiety and somatic comorbidity, respectively.

### Validation Set

Using this model in the validation set showed that the maximum sum of the sensitivity and specificity was achieved at a cutoff model-estimated probability of all cause ED visit of 0.21. Therefore, sensitivity, specificity and accuracy of the model were 63.0%, 68.6% and 67.7%, respectively. Table 5 shows the results from validation set after setting the cutoff point at the point where optimum sensitivity and specificity were reached.

**Table 1.** Comparison between derivation and validation sets

|  | Derivation set<br>(n = 335) | Validation set<br>(n = 167) | P value |
|--|-----------------------------|-----------------------------|---------|
| Age (years)  | 57.5 ± 11.5                 | 58.0 ± 10.7                 | 0.646   |
| Sex (male)   | 227 (67.8)                  | 104 (62.3)                  | 0.222   |
| Marital status (married)                           | 285 (85.1)                  | 140 (83.8)                  | 0.716   |
| Family income (> 300 USD)                          | 261 (77.9)                  | 133 (79.6)                  | 0.657   |
| Educational level (lower than high school diploma) | 229 (68.4)                  | 115 (68.9)                  | 0.909   |
| Body Mass Index (≥ 30 kg/m <sup>2</sup> )          | 266 (79.4)                  | 126 (75.4)                  | 0.313   |
| Living place(urban)                                | 306 (91.3)                  | 154 (92.2)                  | 0.739   |
| Angina type (grade I or II)                        | 216 (64.5)                  | 94 (56.3)                   | 0.075   |
| Total comorbidity score                            | 10.8 ± 6.6                  | 11.2 ± 7.2                  | 0.135   |
| Anxiety score                                      | 5.2 ± 3.3                   | 5.1 ± 3.3                   | 0.993   |
| Depression score                                   | 12.3 ± 7.6                  | 12.3 ± 7.4                  | 0.619   |

**Table 2.** Comparison of input variables between participants with and without emergency department visit in the derivation set

| Baseline characteristics             |                                 | No. (%) of ED visits* | P value |
|--------------------------------------|---------------------------------|-----------------------|---------|
| Gender                               | Male                            | 43 (18.9)             | 0.613   |
|                                      | Female                          | 23 (21.3)             |         |
| Marital status                       | Married                         | 54 (18.9)             | 0.407   |
|                                      | Single/divorced                 | 12 (24.0)             |         |
| Family income                        | < 300 US\$                      | 50 (19.2)             | 0.638   |
|                                      | ≥ 300 US\$                      | 16 (21.6)             |         |
| Educational level                    | Less than high school diploma   | 46 (20.1)             | 0.794   |
|                                      | High school diploma or higher   | 20 (18.9)             |         |
| Body Mass Index (kg/m <sup>2</sup> ) | < 30                            | 50 (18.8)             | 0.416   |
|                                      | ≥ 30                            | 16 (23.2)             |         |
| Living place                         | Urban                           | 62 (20.3)             | 0.403   |
|                                      | Rural                           | 4 (13.8)              |         |
| Chest pain                           | No or non-exertional chest pain | 17 (14.3)             | 0.064   |
|                                      | Grade I and II angina (Q)       | 49 (22.7)             |         |

\* Data is presented as number (percent)

**Table 3.** Comparison of baseline data between participants with or without emergency department visit in derivation set

| Baseline characteristics  | Emergency department visit* |                    | P value |
|---------------------------|-----------------------------|--------------------|---------|
|                           | Positive (n = 66)           | Negative (n = 268) |         |
| Age (years)               | 56.6 ± 12.2                 | 57.7 ± 11.3        | 0.468   |
| Somatic comorbidity score | 13.2 ± 6.5                  | 10.2 ± 5.6         | 0.001   |
| Depression score          | 5.7 ± 4.3                   | 5.1 ± 3.0          | 0.217   |
| Anxiety score             | 9.5 ± 6.6                   | 6.4 ± 6.5          | 0.001   |

\* Data is presented as mean ± SD

**Table 4.** Significant predictors of emergency department visit based on logistic regression analysis for the patients in derivation set

| Predictor                 | P value | Adjusted odds ratio | 95% confidence interval |
|---------------------------|---------|---------------------|-------------------------|
| Sex (male)                | 0.047   | 1.753               | 1.102-2.788             |
| Grade I and II angina     | 0.013   | 1.993               | 1.265-3.138             |
| Anxiety score             | 0.004   | 1.062               | 1.026-1.099             |
| Somatic comorbidity score | 0.002   | 1.062               | 1.029-1.096             |

**Table 5.** Comparison between actual and model-predicted number of emergency department visits in the validation set

|                                    |       | Predicted emergency department visits |     |       |
|------------------------------------|-------|---------------------------------------|-----|-------|
|                                    |       | Yes                                   | No  | Total |
| Actual emergency department visits | Yes   | 17                                    | 10  | 27    |
|                                    | No    | 44                                    | 96  | 140   |
|                                    | Total | 61                                    | 106 | 167   |

## Discussion

The present study showed that six month all cause ED visit rate among the studied Iranian IHD patients reaches to 37%. Also, it suggested that all cause ED visit in patients with IHD shows an increase in male patients with grades I or II of angina, higher concomitant somatic comorbidities and higher anxiety symptoms.

As expected, higher grades of angina symptoms were associated with more probability of all cause ED visit in this study. Angina type is reported to be associated with the prognosis of a IHD patient<sup>20,21</sup> and presence of angina substantially increases the risk of death, MI, heart failure and other cardiovascular events in general population.<sup>22,23</sup>

In addition to angina symptoms, the present study showed other associates with all cause ED visit in IHD patients. Literature reports a gender difference in morbidity related to IHD.<sup>24,25</sup> With similar angina symptoms, women might report greater functional disability compared to men<sup>26,27</sup> while men may experience worse outcome after ED visit for unstable angina.<sup>24</sup> It was found in the present study that men, affected by IHD, irrespective of their other baseline data, are more probable to visit ED for any causes.

Anxiety, from one side, might bring optimism when it prompts an individual to quickly seek treatment for acute cardiac symptoms, and from the other side, may worsen the prognosis of IHD patients. In IHD, anxiety might affect adhering to prescribed medications and lifestyle changes, increase the risk for acute cardiac events and increase the risk for complications after acute coronary syndrome.<sup>28</sup>

In the present study, higher somatic comorbidity was associated with higher probability of six month all cause ED visit in IHD patients. Somatic comorbidities are reported as a powerful predictor of all-cause mortality in patients with established IHD.<sup>29</sup> Co-existing illnesses can potentially alter both the efficacy of therapies and the course of the primary disease.<sup>30</sup> As people age, they are more likely to develop chronic somatic conditions and it is estimated that over 60% of people older than 60 years

have two or more of such chronic illnesses.<sup>31</sup> However, unfortunately, most studies of somatic therapeutics typically focus on the index disease.

Although obesity is a risk factor for IHD development,<sup>32</sup> several studies have shown that it may not have any additional and independent negative effect on the outcome of these patients.<sup>33-35</sup> Similarly in the present study no association was found between BMI and ED visits in patient population. The exact cause of such paradox is not defined and several mechanisms could be suggested. Some studies have suggested that obesity-induced hypercholesterolemia might have anti-inflammatory effect against unbound circulating lipopolysaccharides and hence improve long term outcomes.<sup>36,37</sup> In addition, differences in the effect of various types of obesity on the cardiovascular system could explain other parts of this paradox. Peripheral adiposity (i.e. gynoid obesity) is relatively "inert" regarding metabolic and inflammatory properties. In addition, it has cardiovascular benefits due to an association with lower total body fat content and secretion of adiponectin which has anti-inflammatory, insulin-sensitizing, and antiatherogenic effects.<sup>38</sup> In contrast, abdominal obesity is associated with higher total body fat content, more insulin-resistance, more comorbid associations, and more metabolic and inflammatory activities.

Although according to the literature, in IHD, depression plays a role as an associated factor for hospitalization and mortality,<sup>39,40</sup> no predictive value for depression was found in the present study in prediction of six months all cause ED visit in IHD patients. Similarly, some other investigators found no association between depression and mortality risk in IHD patients.<sup>41</sup>

The current study also presents a method for modeling all cause ED visit and other similar conditions with acceptable sensitivity and specificity. Regarding its reliability and ease of implementation, it is recommended to other healthcare systems, especially in developing countries, to hire such methods.

The presented model is hoped to support

valuable information for healthcare planners. Cardiologists should be more cautious about their male patients, who have higher grade of WHO angina, more somatic comorbid illnesses, and also those with anxiety. In addition, patients may benefit from anxiety reduction interventions and treatment of comorbid conditions. Further research should be conducted to test whether decreased anxiety will decrease ED visit in ACD patients.

It is suggested that further studies assess the efficacy of preventive interventions, with a focus on comorbid conditions and anxiety in ED visits and associated burden and costs in IHD patients.

### Limitations

The disorders of anxiety and depression were

not defined; instead, HADS questionnaire was used to measure these symptoms in present patient population. However, the internal reliability of HADS have been reported to be acceptable.<sup>42</sup> Evaluation of variables only in the beginning of the study, failing to include the cause and timing of ED visits and being single centric are other shortcomings of this study.

### Conclusions

The suggested model with moderate accuracy can be of use for health care providers/planners who are interested to know which patient characteristic affects likelihood of ED visit in IHD patients. However, an external validation of the presented model is needed.

### Conflict of Interests

Authors have no conflict of interests.

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