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Presentation and Symptom Predictors of Coronary Heart Disease in Patients With and Without Diabetes

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The aims of this prospective, observational study were to compare: (1) symptom presentation of coronary heart disease (CHD) between patients with and without diabetes and (2) symptom predictors of CHD in patients with and without diabetes. We directly observed 528 patients with symptoms suggestive of CHD as they presented to the ED of a 900-bed cardiac referral center in the northeastern United States. There were no significant differences in symptom presentation of CHD between patients with and without diabetes, although patients with diabetes were slightly more likely to present with shortness of breath (P = .056). Patients with diabetes reported their symptoms to be more severe compared with those without diabetes (P = .036). Neck/throat pain and arm/shoulder pain were of borderline significance in predicting CHD in patients with diabetes (P = .059 and P = .052, respectively). Classic chest symptoms and diaphoresis were independent predictors of CHD in patients without diabetes (P = .002 and P = .049, respectively). The perceived severity of symptoms was not predictive of CHD in patients with or without diabetes. Symptoms thought to be diagnostic of CHD are not helpful in patients with diabetes. Future research should focus on identifying more useful predictors of CHD in patients with diabetes. (Am J Emerg Med 2001;19:482-487. Copyright © 2001 by W.B. Saunders Company)

According to the American Heart Association, coronary heart disease (CHD) is the single largest killer of Americans. In 1998 alone, 459,841 deaths, or 1 in every 5 deaths in the United States, were attributed to CHD. This year, it is estimated that 1.1 million Americans will have a new or recurrent myocardial infarction (MI) and over 40% of them will die.¹

It is well-established that diabetes mellitus is a strong risk factor for CHD and that CHD represents the most common cause of death for patients with diabetes. In fact, two-thirds of people with diabetes die of some form of heart or blood vessel disease.¹ In patients with MI, diabetes is an important prognostic factor for development of heart failure, recurrent MI, and long-term mortality.²⁻⁷

CHD, however, is often silent in individuals with diabetes.⁸⁻¹² It has been shown that one-quarter of the individuals with diabetes had electrocardiogram (ECG) evidence of

Copyright © 2001 by W.B. Saunders Company 0735-6757/01/1906-0006\$35.00/0 doi:10.1053/ajem.2001.27135 prior unrecognized MI. Half of these individuals had no symptoms, whereas half had atypical symptoms.⁸ In the National Registry of Myocardial Infarction-2 (NRMI-2), diabetes was independently associated with atypical presentation.¹²

The occurrence of asymptomatic ischemia or presentation with atypical symptoms makes diagnosing CHD difficult and may result in a delay in initiating treatment in patients with diabetes.¹³ Therefore, when patients present to the emergency department (ED) with diabetes, there should be a higher index of suspicion for CHD than for patients without diabetes.

Triage in the ED is important in the early identification of patients with potential cardiac problems. The assessment of symptoms is critical to appropriate triage decisions. Increased knowledge of how patients with diabetes present with CHD should enable expeditious and accurate identification of cardiac problems. This should lead to early intervention, as with thrombolytic therapy or primary angioplasty, that should limit infarct size, improve outcomes, and reduce mortality. In fact, it has been found that patients with diabetes receive thrombolytics less frequently than patients without diabetes.^{14,15} Some have suggested that this is because of delayed recognition of symptoms as cardiac in origin by the patient or by the clinician.¹⁵

In this study we sought to answer 2 research questions:

- 1. Is there a difference in symptom presentation of CHD between patients with and without diabetes?
- 2. Is there a difference in symptom predictors of CHD between patients with and without diabetes?

We hypothesized that: (1) patients with diabetes will be more likely to present with atypical symptoms compared with patients without diabetes; (2) typical symptoms will be predictive of CHD in both patients with diabetes and patients without diabetes; and (3) atypical symptoms will be predictive of CHD in patients with diabetes, but not in patients without diabetes.

METHODS

Setting and Sample

We did a secondary analysis of data we collected for a larger prospective study in which we examined various aspects of symptom presentation of CHD.¹⁶⁻¹⁸ We observed patients with symptoms suggestive of CHD as they presented to the ED of a 900-bed cardiac referral center in the northeastern United States. Patients were observed if they were \geq 45 years of age and reported at least one symptom suggestive of CHD (Table 1). Additionally, patients

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Key Words: Diabetes, coronary heart disease, presenting symptoms.

TABLE 1. Presenting Symptoms Suggestive of Coronary Heart Disease

Typical Symptoms
Substernal chest pain (not related to trauma)
Left-sided chest pain (not related to trauma)
Chest pressure
Chest heaviness
Tightness or squeezing in chest
Neck or throat pain or discomfort (not related to trauma)
Jaw pain or discomfort (not related to toothache or trauma)
Shoulder pain or discomfort (not related to degenerative joint disease or trauma)
Arm pain or discomfort (not related to bursitis or trauma)
Diaphoresis
Shortness of breath (not related to asthma, pulmonary infection, pre-existing pulmonary problem, or renal failure)
Atypical Symptoms
Chest pain in other location
Fullness in chest
Stabbing in chest
Numbness, tingling, or pricking in chest
Burning in chest
Epigastric/indigestion-like/gas-like pain or discomfort (not related to gastrointestinal problem)
Nausea or vomiting (not related to gastrointestinal problem)
Upper extremity numbness or tingling (not related to stroke or carpel tunnel problem)
Midback (between shoulder blades) pain (not related to degenerative joint disease or trauma)
Pain/discomfort with deep breath (not related to asthma, pulmonary infection, or pre-existing pulmonary problem)
Cough (not related to asthma, pulmonary infection, or pre-existing pulmonary problem)
Dizziness, lightheadedness (not related to stroke, neurologic problem, or hypertension)
Syncope (not related to stroke, neurologic problem, or hypertension)
Fatigue or weakness (not related to stroke, neurologic problem, or hypertension)
Palpitations (new onset, no history of arrhythmias)

18 to 44 years were asked to participate if they had diabetes or at least 2 cardiac risk factors (history of CHD, systemic hypertension, hypercholesteremia, smoking, obesity, family history of premature CHD, and postmenopausal state), and at least one symptom suggestive of CHD. We included these additional criteria for younger patients to exclude patients at very low risk for CHD. A total of 536 patients met study criteria and were approached for participation. Of these, 531 patients agreed to participate (<1% refusal rate). Information on diabetes status was missing on 3 patients, resulting in a final sample size of 528.

Procedure

This study was approved by the appropriate institutional review boards. Between September 1995 and August 1997 during shifts of 2 to 5 hours across all 24 hours and all 7 days, nurse data collectors unobtrusively observed all patients meeting study criteria as they presented to the ED. The data collector approached the patient for oral consent after the ED staff completed the initial assessment of the patient and caregiving activities allowed. In the event that patients were too sick to provide oral consent in the ED, patients were approached when they were considered stable and were within 24 hours of hospital admission. No patient died before obtaining consent.

Data on presenting symptoms were obtained by observing the patient-physician or patient-nurse interview, and symptoms were documented verbatim. Data on baseline characteristics (demographics, preexisting health conditions, and cardiac risk factors) were gathered from the patient and the medical record. Data on severity of symptoms were obtained by asking the patient to identify the number on a scale of 0 to 10 for the worst physical discomfort they experienced on that day, where 0 was none at all and 10 was the worst the patient could imagine. The presence of diabetes mellitus was determined by asking the patient or family, or from the medical record, and it was coded as either present or absent. We did not have information on the type of diabetes (type 1 or type 2). CHD was determined by standard ECG and enzyme criteria. CHD was defined as either acute ischemia or acute MI. Acute ischemia was determined by ECG evidence of ST-segment depression, ST-segment elevation, or T-wave inversion or T-wave abnormalities different from the last ECG in at least 2 consecutive leads and lack of cardiac enzyme elevation. Elevated cardiac enzymes (CK-MB >5% of total CK in at least one set) indicated acute MI. Interrater agreement checks were done bimonthly during the 2 years of data collection and were always above 95%.

Statistical Analyses

Data were analyzed using SAS Version 8 statistical software (SAS, Cary, NC). For both research questions, only symptoms that were reported by >5% of the sample were included in the analyses. Because some symptoms are clinically similar and to ensure adequate numbers for analyses, we combined some symptoms into a single variable. Typical symptoms included classic chest symptoms as a single variable (pain, pressure, heaviness, tightness, or squeezing in the center or left chest), neck or throat pain, jaw pain, arm or shoulder pain, diaphoresis, or shortness of breath. Atypical symptoms included atypical chest symptoms as a single variable (fullness, stabbing, numbness, or burning in the chest or pain in the right chest), epigastric discomfort, nausea or vomiting, upper extremity numbness or tingling, midback pain, pain with deep breath, cough, dizziness or syncope, fatigue or weakness, and palpitations.

To address research question 1, we used chi-square analysis to examine differences in symptom presentation of CHD between patients with and without diabetes (n = 215 patients with CHD). We performed a t-test to compare the mean rating of severity of symptoms between patients with and without diabetes. We then used multiple regression, with an alpha level of .20 for entering and staying in the model, to control for factors that could have an impact on perceived severity of symptoms. These included history of heart failure, age, gender, prior diagnosis of CHD, psychiatric history, and smoking.

To address research question 2, we did separate analyses for the subgroups of patients with (n = 142) and without (n = 386)

diabetes. Initially, we used chi-square analysis to determine symptoms associated with CHD. Then to determine independent symptom predictors of CHD in patients with and without diabetes, we performed stepwise logistic regression analysis in each group. We entered all typical and atypical symptoms reported by >5% of the sample and forced in age and gender as control factors. We used an alpha level of .20 for entering and staying in the model and confirmed our results by forward selection and backward elimination modeling. We used t-test analyses to compare the mean rating of severity of symptoms between patients with and without CHD in the group of patients with diabetes and in the group without diabetes.

RESULTS

Of a total sample of 528 patients, 215 were ultimately diagnosed with CHD for their ED visit, 142 had diabetes, and 66 had CHD and diabetes.

Symptom Presentation of CHD in Patients With and Without Diabetes

To address our first research question regarding differences in symptom presentation of CHD between patients with and without diabetes, we examined data from the 215 patients in the sample who were diagnosed with CHD (80 with acute MI and 135 with acute ischemia). A majority of these patients with CHD were white (73.5%) and men (58.6%). Ages ranged from 30 to 96, with a mean age of 65.9 ± 14.8 years. We compared presenting symptoms in the 66 with diabetes with presenting symptoms in the 149 who did not have diabetes.

As shown in Table 2, there were no statistically significant differences in symptom presentation between patients

TABLE 2. Differences in Symptom Presentation of Coronary Heart Disease Between Patients With and Without Diabetes by Chi-Square Analysis (N = 215)

by Chi-Square Analysis (N = 215)						
Symptom	Diabetes (n = 66) N (%)	No Diabetes (n = 149) N (%)	P			
Typical Symptoms						
Shortness of breath	34 (51.5%)	56 (37.6%)	.056			
Neck/throat pain	9 (13.6%)	11 (7.4%)	.145			
Diaphoresis	14 (21.2%)	40 (26.9%)	.380			
Classic chest symptoms (pain, pressure, heaviness, tightness, or squeezing in center or left chest) Jaw pain Arm/shoulder pain Atypical Symptoms Atypical chest symptoms (fullness, stabbing, numbness, or burning in chest or pain in right	45 (68.2%) 5 (7.6%) 21 (31.9%)	106 (71.1%) 8 (5.4%) 46 (30.9%)	.662 .752 .890			
chest)	5 (7.6%)	18 (12.1%)	.324			
Nausea/vomiting	17 (25.8%)	30 (20.1%)	.357			
Dizziness/syncope	11 (16.7%)	31 (20.8%)	.480			
Fatigue/weakness	10 (15.2%)	18 (12.1%)	.537			
Palpitations	5 (7.6%)	8 (5.4%)	.752			
Epigastric discomfort	10 (15.2%)	24 (16.1%)	.859			
Midback pain	4 (6.1%)	10 (6.7%)	.999			

with diabetes and patients who did not have diabetes. Although the differences in the occurrence of shortness of breath did not reach statistical significance, there was a notable trend. Of the patients with diabetes, 51.5% experienced shortness of breath, in contrast to only 37.6% of those without diabetes (P = .056). To determine if chest symptoms as a whole occurred more often in patients without diabetes, we combined all classic chest symptoms (pain, pressure, heaviness, tightness, or squeezing in the center or left chest) into one variable. Although slightly more patients without diabetes presented with classic chest symptoms (71.1%) compared with patients with diabetes (68.2%), this difference was not statistically significant (P = .662). Likewise, we also combined all atypical chest symptoms (fullness, stabbing, numbness, or burning in the chest or pain in the right chest) into one variable. More patients without diabetes presented with these atypical chest symptoms (12.1%) compared with patients without diabetes (7.6%), but this difference was not statistically significant (P =.324).

Using the 0 to 10 scale, patients with diabetes (mean = 7.51 ± 2.20) rated their symptoms as significantly more severe than did those without diabetes (mean = 6.68 ± 2.58 ; P = .042). The relationship between diabetes and severity of symptoms remained significant (P = .036) even when using multiple regression to control for factors that could have an impact on perceived severity of symptoms. It is important to note, however, that only 173 of the 215 patients with CHD (80.5%) were able to quantify the severity of their symptoms using the 0 to 10 scale. We found that older patients were less likely to be able to quantify the severity of their symptoms. The mean age of those unable to rate symptoms was 73.4 ± 15.2 years, whereas the mean age of those who did rate their symptoms was 64.1 ± 14.2 (P = .0002).

Symptom Predictors of CHD in Patients With and Without Diabetes

To address our second research question regarding which symptoms are predictive of CHD in patients with and without diabetes, we examined data first from the subgroup with diabetes (n = 142) and then from the subgroup without diabetes (n = 386).

Patients With Diabetes

Of the 142 patients with diabetes, 70.4% were white and 48.6% were men. Ages ranged from 32 to 93, with a mean age of 65.3 ± 13.7 years. We compared the 66 patients who were diagnosed with CHD with the 76 who were not diagnosed with CHD.

As shown in Table 3, neck/throat pain and arm/shoulder pain were significant (P < .05) bivariate predictors of CHD in patients with diabetes. In these patients, 82% of those with neck or throat pain were diagnosed with CHD, in contrast to 44% of patients without this symptom (P = .014). In addition, 64% of patients with arm or shoulder pain were diagnosed with CHD, compared with 41% of patients without this symptom (P = .024). No other symptoms were significantly related to the diagnosis of CHD in patients with diabetes.

To identify the most important symptom predictors in the presence of many typical and atypical presenting symptoms, we entered all symptoms into a logistic regression analysis,

TABLE 3.	Bivariate Symptom	Predictors of Cor	onarv Heart	Disease in F	Patients W	Vith and W	/ithout Diabetes

Symptom	Patients With Diabetes $(N = 142)$			Patients Without Diabetes $(N = 386)$		
	Symptom Present	Symptom Absent	P	Symptom Present	Symptom Absent	Р
Typical Symptoms						
Neck/throat pain	82%	44%	.014	36%	39%	.710
Arm/shoulder pain	64%	41%	.024	40%	38%	.648
Classic chest symptoms (pain, pressure,						
heaviness, tightness, or squeezing in						
center or left chest)	51%	39%	.155	43%	31%	.016
Diaphoresis	54%	45%	.405	47%	36%	.087
Jaw pain	42%	47%	.727	50%	38%	.339
Shortness of breath	48%	45%	.736	40%	38%	.610
Atypical Symptoms						
Dizziness/syncope	39%	48%	.394	32%	41%	.101
Epigastric discomfort	56%	45%	.409	37%	39%	.761
Fatigue/weakness	40%	48%	.474	38%	39%	.867
Palpitations	63%	46%	.568	25%	40%	.100
Nausea/vomiting	47%	46%	.918	40%	38%	.782
Atypical chest symptoms (fullness,						
stabbing, numbness, or burning in chest						
or pain in right chest)	45%	47%	.944	41%	38%	.738
Midback pain	44%	47%	.999	37%	39%	.863

while controlling for age and gender. Both neck/throat pain and arm/shoulder pain achieved borderline significance in predicting CHD (P = .052 and P = .059, respectively; see Table 4).

In patients with diabetes, the perceived severity of symptoms did not differ between those who were diagnosed with CHD for their ED visit and those who were not (P = .504). Again, it is important to note that only 113 of the 142 patients with diabetes (79.6%) were able to quantify the severity of their symptoms using the 0 to 10 scale.

Patients Without Diabetes

Of the 386 patients without diabetes, 73.8% were white and 54.7% were men. Ages ranged from 22 to 96, with a mean age of 62.5 ± 16.3 years. We compared the 149 patients who were diagnosed with CHD with the 237 who were not diagnosed with CHD.

As shown in Table 3, the combined variable of classic chest symptoms was the only significant (P < .05) bivariate predictor of CHD in patients without diabetes. In patients

without diabetes, 43% of patients presenting with classic chest symptoms were diagnosed with CHD, as compared with 31% of patients who did not have classic chest symptoms (P = .016).

In this group of patients without diabetes, we entered all symptoms into a logistic regression analysis, while controlling for age and gender, to determine the most important symptom predictors of CHD in the presence of many typical and atypical presenting symptoms. After taking these other factors into account, classic chest symptoms was found to be a significant predictor of CHD (P = .002; see Table 4). The odds ratio indicates that patients presenting with classic chest symptoms are twice as likely to be diagnosed with CHD, compared with patients without these symptoms (adjusted odds ratio = 2.10; 95% confidence interval = 1.31 - 3.37). Diaphoresis was also found to be a significant predictor of CHD (adjusted odds ratio = 1.68; 95% confidence interval = 1.00 - 2.81; P = .049).

As in patients with diabetes, in patients without diabetes the perceived severity of symptoms did not differ between

TABLE 4. Independent Symptom Predictors of Coronary Heart Disease in Patients With and Without Diabetes by Logistic Regression

 Analysis

Adjusted Odds Ratio*	95% Confidence Interval	Р
2.39	0.99-5.72	.052
4.82	0.94-24.64	.059
2.10	1.31-3.37	.002
1.68	1.00-2.81	.049
1.68	0.85-3.35	.138
	Odds Ratio* 2.39 4.82 2.10 1.68	Odds Ratio* Interval 2.39 0.99-5.72 4.82 0.94-24.64 2.10 1.31-3.37 1.68 1.00-2.81

* Controlled for age and gender

those who were diagnosed with CHD for their ED visit and those who were not (P = .559). Again, it is important to note that only 303 of the 386 patients with CHD (78.5%) were able to quantify the severity of their symptoms using the 0 to 10 scale.

DISCUSSION

The results of our study suggest that symptoms of CHD are similar for patients with and without diabetes, however those with diabetes reported their symptoms to be more severe. Neck/throat pain and arm/shoulder pain were of borderline significance in predicting CHD in patients with diabetes. Classic chest symptoms and diaphoresis were independent predictors of CHD in patients without diabetes. The perceived severity of symptoms was not predictive of CHD in patients with or without diabetes. Thus, our data do not support our hypotheses that: (1) patients with diabetes will be more likely to present with atypical symptoms compared with patients without diabetes; (2) typical symptoms will be predictive of CHD in both patients with diabetes and patients without diabetes; and (3) atypical symptoms will be predictive of CHD in patients with diabetes, but not in patients without diabetes.

Symptom Presentation of CHD in Patients With and Without Diabetes

Previous research suggests that individuals with diabetes are more likely to have silent ischemia and are more likely to experience a silent MI compared with individuals without diabetes.⁸⁻¹² In the setting of acute MI, some researchers have found that people with diabetes are less likely to experience ischemic chest pain and have suggested that this may be related to the presence of cardiovascular autonomic neuropathy.^{9,12,19} Others, however, have shown that chest pain was seen with equal frequency in people with and without diabetes²⁰ or only slightly less often in individuals with diabetes.^{21,22}

Because inclusion criteria for our study required patients to have symptoms suggestive of CHD, we cannot comment on the incidence of silent ischemia or silent MI. Regardless of diabetes status, patients in our sample were equally likely to present with chest symptoms. When we combined all classic chest symptoms together, there was no significant difference in the occurrence of classic chest symptoms between those with and without diabetes (68.2% v 71.1%, respectively; P = .662). In a study of 7,157 patients presenting to the ED, Herlitz et al²² found that chest pain occurred slightly less often in patients with diabetes than in those without diabetes (90% v 93%, respectively; P < .05). Our smaller sample size (n = 215 with CHD), and resulting lower statistical power, may account for the lack of observed statistical difference in the occurrence of classic chest symptoms in patients with and without diabetes in our study.

Findings from our study also do not indicate that patients with diabetes are more likely to present with atypical symptoms. There was no significant difference in the occurrence of atypical chest symptoms between those with and without diabetes (P = .324). Although more patients with diabetes presented with shortness of breath, the difference did not quite reach statistical significance (P = .056). A potentially

higher incidence of shortness of breath in patients with diabetes may be related to a higher incidence of heart failure that is frequently found in individuals with diabetes on presentation with acute ischemia.^{7,21,22} Herlitz et al²² also found pulmonary and pleural symptoms more frequently in patients with diabetes, however, the difference was not statistically significant and prevalence was far less than in the present investigation. In addition, Herlitz et al²² did not assess other symptoms in as great detail as in the present study.

In the present study, patients with diabetes rated the severity of their symptoms higher than patients without diabetes. This finding is contrary to the cardiovascular autonomic neuropathy hypothesis. In our sample, we did not have any information on physiologic indicators of cardiovascular autonomic neuropathy, nor did we know about degree of glycemic control or duration of diagnosis of diabetes. This finding of increased severity of symptoms could be reflective of more extensive cardiac disease and the compounding effect of multiple system involvement in patients with diabetes, compared with patients without diabetes. In addition, we considered not only pain, but many types of symptoms.

It is important to note, however, that not all patients with CHD were able to quantify the severity of their symptoms using the 0 to 10 scale. Therefore, we may not be able to generalize our findings to the whole population of patients with CHD. In particular, the increased perceived severity of symptoms may not be true in older patients, many of whom were unable to quantify the severity of their symptoms using the 0 to 10 scale. Although our information on the severity of symptoms is limited, it is the first time that this has been examined in this population of patients. Further investigation regarding differences in perception of severity of symptoms between those with and without diabetes is indicated.

Symptom Predictors of CHD in Patients With and Without Diabetes

Logistic regression analysis revealed that neck/throat pain and arm/shoulder pain were of borderline significance in predicting CHD in patients with diabetes. Even when we combined pain, pressure, heaviness, tightness, or squeezing in the center or left chest into one variable, we found that these classic chest symptoms were not predictive of CHD in patients with diabetes. On the other hand, the presence of classic chest symptoms and diaphoresis were independent predictors of CHD in patients without diabetes.

No previous investigations have examined symptom predictors of CHD in patients with diabetes. Likewise, there is little research-based knowledge of symptom predictors of CHD in the general population, although the nomenclature of "classic" and "typical" used in reference to certain symptoms indicates that we consider these symptoms to be predictive of CHD. Indeed, our results support the association of classic chest symptoms and diaphoresis with CHD in patients without diabetes.

Strengths and Limitations

There are several strengths and limitations that may influence the interpretation of our findings. Strengths include our prospective, observational design in which detailed data on presenting symptoms were collected by direct observation in the ED. This approach minimizes recall bias on reporting of symptoms and maximizes accuracy. The potential problem of health care professionals interpreting patients' symptoms and recording medical terms is avoided. Second, we considered all types of typical and atypical symptoms suggestive of CHD, not just chest pain. Lastly, this is the first study to examine symptom predictors of CHD among patients with and without diabetes.

Limitations include the relatively small number of patients with diabetes who were diagnosed with CHD. This may have resulted in the lack of observed differences in most of the symptoms between patients with and without diabetes. Larger studies are needed to examine differences in symptom presentation and to determine symptom predictors of CHD in patients with diabetes. Second, we did not have data on the type of diabetes (type 1 or type 2), the degree of glycemic control, or indicators of cardiovascular autonomic neuropathy. Also, some patients with diabetes may not have been diagnosed yet, and thus they were included in the group without diabetes. In addition, sample size limitations required that we collapse patients with acute ischemia and MI into one group for the analyses, thus precluding an analysis of presenting symptoms in patients with acute MI.

CONCLUSIONS

With these strengths and limitations in mind, we can conclude that there were more similarities than differences in symptom presentation of CHD between patients with and without diabetes, although patients with diabetes reported their symptoms to be more severe compared with those without diabetes. Neck/throat pain and arm/shoulder pain were of borderline significance in predicting CHD in patients with diabetes. Classic chest symptoms and diaphoresis were independent predictors of CHD in patients without diabetes. Clinicians need to be aware that patients with diabetes can present with a wide variety of symptoms and that symptoms thought to be diagnostic of CHD are not helpful in patients with diabetes. Future research should focus on identifying more useful predictors of CHD in patients with diabetes.

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