DIABETES/METABOLISM RESEARCH AND REVIEWS
Diabetes Metab Res Rev 2002; **18**: 201–208.
Published online in Wiley InterScience (www.interscience.wiley.com). **DOI:** 10.1002/dmrr.297

REVIEW ARTICLE

Diagnosing coronary artery disease in diabetic patients

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Received: 29 October 2001
Revised: 5 March 2002
Accepted: 8 March 2002

Summary

Although several diagnostic modalities are available to the clinician interested in diagnosing coronary artery disease, very few have been validated in diabetic populations. This review discusses the non-invasive diagnosis of coronary disease in diabetic patients. Evidence regarding the prevalence and prognostic significance of silent ischemia is reviewed and the potential impact of silent ischemia on the diagnostic characteristics of the exercise treadmill test discussed. Other diagnostic tools are considered, and recommendations are made with respect to screening asymptomatic diabetic patients for coronary artery disease. Copyright © 2002 John Wiley & Sons, Ltd.

Keywords coronary artery disease; diabetes; exercise testing; diagnosis

Introduction

Several diagnostic modalities are available to the clinician interested in diagnosing coronary artery disease. However, very few of these have been validated in diabetic populations. For example, the value of exercise testing, the central diagnostic test of the cardiologist, is unknown in the diabetic population. Surprisingly, few studies have examined exercise testing with angiographic endpoints only in diabetic patients, and fewer still have related baseline exercise test characteristics to events. In light of the recent upturn of interest in the cardiovascular well-being of the diabetic population [1] and the demonstration of major benefits from control of cardiovascular risk factors, some have gone as far as to suggest that diabetes be viewed as a cardiovascular disease [2].

That both type 1 and type 2 diabetes are independent risk factors for coronary heart disease is well known [3,4]. In addition to atherosclerotic disease, however, diabetic patients develop disproportionate ventricular dysfunction (diabetic cardiomyopathy) [5–9]. This encompasses systolic and diastolic dysfunction, the causes of which are thought to include atherosclerosis, prolonged hypertension, chronic hyperglycemia, microvascular disease, glycosylation of myocardial proteins, and autonomic neuropathy [2]. In addition, studies suggest that diabetic patients are more prone to 'silent' or asymptomatic disease [9–11] which is associated with later presentation, and possibly poorer prognosis.

The exercise test has remained at the heart of the work-up of the cardiac patient since it was first proposed by Goldhammer and Scherf [12]. Much of its diagnostic power relies on changes in the ST segment with exercise, the mechanism for which has only recently come to light [13]. However, several studies have shown high diagnostic discriminatory value for exertional chest pain as a cause of termination of the exercise test [14,15]. Clearly, the presence of silent ischemia calls for separate assessment of exercise test characteristics in the diabetic population.

In addition to diagnostic applications, recent publications have emphasised the utility of the exercise test for risk assessment and prognosis [16,17]. The focus on new variables and the addition of gas analysis to the basic test can add valuable information that may have particular relevance for the mixed aetiology of diabetic cardiovascular disease.

For those patients in whom exercise testing is inconclusive or not appropriate, however, several alternative diagnostic modalities exist. Most can provide information on regional ischemia and can quantify left ventricular dysfunction. If exercise rather than pharmacological stress is used, information on exercise capacity, the variable often found to have the highest predictive power in determination of risk, can also be obtained.

Screening concepts

Definition of screening

Screening can be defined as the presumptive identification of unrecognized disease. The value of any screening test depends on several key principles: that the target disease has an asymptomatic period during which its outcome can be altered; that screening tests and interventions are acceptable to patients; that quantity or quality of life can be favorably altered; that sufficient resources are available for both screening and intervention; and that the screening test displays sufficiently high sensitivity and specificity to justify its expense. We know that diabetic cardiovascular disease fulfils many of these requisites.

Bayes legacy

A basic step in the application of any testing procedure for the separation of diabetic patients with heart disease from those without is to determine the optimal cutpoint value. Unfortunately, most tests involve considerable overlap. If the value is set to identify nearly all the normal subjects as being free of disease (e.g. 0.2 mV of ST-segment depression), the test will have a high specificity. However, a substantial number of those with disease will also be called normal. If a value is chosen far in the opposite direction (e.g. 0.05 mV ST-segment depression), nearly all those with disease are identified as being abnormal, giving the test a high sensitivity, but many normal subjects are also identified as abnormal. Self evidently, a cutpoint value that equally mislabels the normal subjects and those with disease will have the highest predictive accuracy.

However, there may be reasons for adjusting a test to have higher sensitivity or specificity than that which optimizes predictive accuracy. For instance, sensitivity should be highest in the emergency room and specificity highest when doing insurance exams. Tests aimed at improving diagnostic power by assessing test characteristics for a variety of cutpoints are available (receiver operating characteristic [ROC] analysis).

Since the percentage of those with an abnormal test who will have disease (positive predictive value) is dependent on the pre-test prevalence of disease, identifying a subpopulation with a higher prevalence of disease can improve the test characteristics. This is the natural extension of Bayes theorem. From a screening perspective, however, is it reasonable to consider that the longer diabetes has been present and the poorer the glycemic control, the more likely we are to find heart disease? Or that the presence of other diabetic complications will be associated with a higher prevalence of heart disease? At what point do these markers sufficiently increase the pre-test probability in diabetic patients as to make screening appropriate and cost-effective [18–21]?

Multiple endpoints

The associated endpoints of atherosclerotic and cardiomyopathic disease may have independent predictors, yet it can be difficult to distinguish between them. This is compounded by the use of overlapping endpoints in some studies (e.g. ischemic heart disease, cardiovascular disease). In addition, while microangiopathic disease results in diastolic and systolic dysfunction, it is not known to cause ischemia that can be detected by electrocardiography (ECG) or nuclear exercise testing, leaving echocardiography as the only screening test currently widely available for microangiopathic cardiomyopathy [cardiovascular magnetic resonance imaging (MRI) may well supersede echo in time]. The established tests for ischemia caused by atherosclerosis in larger arteries are the exercise ECG and nuclear stress perfusion.

Silent ischemia: more common in diabetic patients?

Several studies have suggested that exercise-induced silent ischemia is more common in diabetic patients than in the general population. Nesto *et al*. found 14/50 diabetic patients but 34/50 non-diabetic patients with ischemia experienced angina during exercise thallium scintigraphy [22], while Naka *et al*. [23] demonstrated that among patients with abnormal angiograms, diabetic patients had a prevalence of silent myocardial ischemia that was 2.2 times higher than that of non-diabetic control subjects. Interestingly, in this latter study, diabetic patients who received insulin had a 2.6 times greater prevalence of silent myocardial ischemia than those who did not (a similar association with retinopathy and, in another study, with microalbuminuria was also present [24]).

Autonomic dysfunction: a mechanism

Autonomic dysfunction has for some time been thought to be the most likely mechanism to explain silent ischemia in diabetic patients. Only more recently, however, has experimental data been available to support this suggestion. Hikita *et al*. [25] showed that beta-endorphin levels and heart rate (HR) variability during exercise were significantly greater in non-diabetic patients with silent ischemia than in diabetic patients, whilst Marchant *et al.* [26] found that patients with exercise silent ischemia were more often diabetic (33% vs 63%), had a prolonged time to ischemia, and suffered impairment of autonomic function (Valsalva ratio, supine/standing HR ratio). Subgroup analysis showed that abnormalities of autonomic function were confined to the diabetic patients. Langer examined pain threshold measurements and their relation to silent myocardial ischemia [27]. Of 58 diabetic patients, 21 were found to have autonomic dysfunction (36%). Furthermore, although silent myocardial ischemia was detected in ten patients (17%), and was significantly more frequent in patients with than without autonomic dysfunction (38% vs 5%), there was no difference in the electrical pain threshold or tolerance in subjects with and without silent myocardial ischemia. Together these studies suggest a clear role for neuropathy in silent ischemia. In particular, the last study suggests that neuropathy is more important than central pain pathways.

Silent ischemia: not more common in diabetic patients?

In contrast, some studies have failed to show a difference in the prevalence of silent myocardial ischemia between diabetic patients and the general population. In a landmark Danish study [28], the prevalence of ischemia was compared in a random sample of 120 users of insulin and 120 users of oral hypoglycemic agents aged 40–75 years. The observed prevalence of silent ischemia on treadmill or Holter testing in diabetic patients was 13.5% and was no different in matched controls. No association was found between silent ischemia and gender or diabetes type. Although hypertension was highly predictive of silent ischemia in the diabetic subjects, other variables did not have a predictive value. This finding is hard to explain. Scandinavian populations have previously been noted to outlie in cardiovascular disease prevalence [29] and it is possible that a high level of baseline disease in the non-diabetic population masks the population differences seen in other studies.

Data from the Asymptomatic Cardiac Ischemia Pilot [30] revealed that asymptomatic ST-segment depression during Holter monitoring was 94% in diabetic patients and 88% in non-diabetic controls. In addition, the time to onset of 1 mm ST-segment depression and time to onset of angina were similar in both groups. Unlike the previous study, however, entry into the ACIP required a cardiac event so the disease was not consistently silent.

Silent ischemia: prognosis

Several studies have focused on the prognostic implications of silent ischemia regardless of diabetic status. In the Coronary Artery Surgery Study (CASS), patients who underwent coronary angiography and exercise testing were followed for 7 years [31]. Four hundred and twenty-four had ischemic ST-segment depression without angina; 232 had angina but no ischemic ST segment depression; 456 had both ischemic ST segment depression and angina; and 471 had neither ischemic ST depression nor angina. Notably, the 7-year survival rates were similar for patients in all groups (77%) except for patients without ST-segment depression or angina who did better (88%). Furthermore, a subgroup analysis of 424 patients with proven coronary disease showed that those with silent ischemia had similar risk of myocardial infarction (MI) or sudden death as those with symptomatic ischemia, (except in those with three-vessel disease, where silent ischemia was associated with greater risk) [32]. This mirrors work from the Framingham study where of 708 MIs among 5127 participants, risk estimate comparisons showed that unrecognized infarctions were as likely as recognized infarctions to cause death, heart failure or stroke. Taken together, these findings raise the question of screening: if unrecognized disease has similarly poor prognosis to recognized disease, if a screening test exists and, in the case of diabetic patients, if the disease is found at a sufficiently high prevalence, then a case can be made for screening asymptomatic sufferers.

Some authors, however, have found prognostic differences between symptomatic and asymptomatic exercise-induced ischemia in the general population. Mark *et al.* [33] analyzed 1698 consecutive patients with symptomatic coronary artery disease and found that silent ischemia during treadmill testing indicated a subgroup of patients who had a less aggressive anginal course, less coronary artery disease by angiography, and a better prognosis. Other smaller angiographic studies agree with this finding [34–38] which may reflect the bluntness of the tool that is exercise-induced ST depression. It is possible that those with no pain had less severe disease despite similar levels of ST depression.

Some studies have taken account of diabetic status in assessing silent ischemia. In 1989, we attempted to determine the prognosis of silent ischemia in consecutive patients referred for exercise testing [39]. Secondarily, we assessed whether age, MI or diabetes mellitus influenced the prevalence of silent myocardial ischemia during exercise testing. We found the same prevalence of silent ischemia in diabetic patients as non-diabetic controls (c. 60%). Our primary finding was that the mortality rate was significantly greater among patients with abnormal ST-segment depression than in patients without ST-segment depression. The presence or absence of angina pectoris during exercise testing was not significantly related to death and the prevalence of silent ischemia was not significantly different among patients with MI or diabetes, but was directly related to age. In contrast, Weiner *et al.* [40] found the 6-year survival among patients with silent ischemia was worse in diabetic than non-diabetic patients (59% vs 82%, respectively), although the 6-year survival among patients without ischemia was similar among diabetic and non-diabetic patients.

Making sense of these seemingly contradictory findings is not straightforward. Silent myocardial ischemia has been found to be associated with the same, lower, and higher risk as non-silent ischemia. It has been found to occur with the same and higher frequency in diabetic patients. What is clear, however, is that whether silent or not, ischemia during treadmill testing in the general population predicts increased risk for death. However, in general these study patients presented for testing *with chest pain symptoms*. That is, their ischemia was 'silent' only in respect of the exercise test itself. This inconsistent appearance of pain could represent a different process in the general population (e.g. a different severity of disease) than in the diabetic population, where autonomic dysfunction is known to be present. This idea is supported by Weiner's studies, in which patients with silent ischemia and either three-vessel disease [32] or diabetes [40] had a poorer outcome.

Screening studies

The inherent uncertainty of assessing the prevalence and risk of silent coronary artery disease retrospectively has led some investigators to assess the impact of truly silent disease by carrying out prospective screening studies. We found only four studies that took a truly asymptomatic diabetic population and screened for cardiovascular disease. Koistinen *et al*. [41] found 29% of diabetic patients and 5% of controls had ischemic results in one or more non-invasive tests whilst Gerson and colleagues [42] found one-quarter of 110 asymptomatic, insulin-requiring diabetic patients had abnormal ST depression or an inadequate HR response. More recently, Janand-Delenne *et al*. [43] found 16% of non-invasive tests to be positive in 203 patients screened for 1 year with exercise ECG and thallium myocardial scintigraphy followed up with coronary angiography. Angiographically significant (>50% stenosis) disease was found in 9.3% of patients. Finally, May *et al*. [28] found the prevalence of silent ischaemia to be 13.5% in a randomly chosen diabetic population.

It seems likely then that the prevalence of silent cardiovascular disease in diabetic populations is high, and probably of the order of 10–30%, compared with a control rate of around 5%. However, the diagnostic tools available to assess coronary disease in the general population need to be re-evaluated for the diabetic population, in light of the significantly higher pre-probability of disease, and the potential confounding factor of silent ischemia.

Which screening test?

Several tools are available for the diagnosis of cardiovascular disease (Table 1). Although the exercise treadmill test occupies a central role in the work-up of the coronary disease, ST depression cannot localize the disease to the territory of one coronary artery over another. Imaging tests clearly *are* able to localize ischemia as well as diagnose coronary disease when lack of mobility precludes an exercise test or when the baseline ECG prohibits ST analysis (such as in the presence of more than 1 mm resting ST depression, left bundle branch block, or Wolf-Parkinson-White syndrome). However, it should be noted that, traditionally, coronary angiography has been taken as the gold standard used to derive sensitivity and specificity estimates. Angiography can, however, only detect macrovascular disease. In addition, the relationship between the severity of narrowing and risk is not straightforward [44]. In addition, imaging strategies have been shown to be associated with incremental prognostic data over and above angiographic variables [45].

Exercise testing

In the study of Gerson *et al*. [42] discussed above, although baseline variables that were univariately predictive of subsequent clinical coronary disease in diabetic

Table 1. Comparison of tests used in the diagnosis of coronary artery disease[a]

Grouping	Studies (*n*)	Total patients (*n*)	Sensitivity (%)	Specificity (%)	Predictive accuracy (%)
Meta-analysis of standard exercise ECG	147	24 047	68	77	73
Excluding MI patients	41	11 691	67	72	69
Limiting work-up bias	2	>1000	50	90	69
Meta-analysis of exercise test scores	24	11 788			80
Probability stratification of exercise test scores	1	2000	95	90	92
Thallium scintigraphy	59	6038	85	85	85
SPECT without MI	27	2136	86	62	74
Exercise echocardiography	58	5000	84	75	80
Exercise echocardiography excluding MI patients	24	2109	87	84	85
Non-exercise stress tests					
Persantine thallium	11	<1000	85	91	87
Dobutamine echocardiography	5	<1000	88	84	86
CKG	1	617	71	88	79
EBCT	5	2373	90	45	61

[a]Values shown for non-exercise stress tests are probably overestimates as a result of work-up bias. CKG is a simple motion sensor that permits recording of the movement of the left ventricle using a small transducer placed on the chest wall. Signal averaging has recently enhanced this technology.
CKG, Cardiokymography; EBCT, electron beam computed tomography; MI, myocardial infarction; SPECT, single photon emission computed tomography.

patients included age, maximal HR, and retinal neovascularization, in multivariate analysis the treadmill HR was the single most important predictor of subsequent clinical coronary disease. A treadmill ECG result that was either abnormal or inconclusive because of failure to achieve 90% of predicted maximal HR, identified each patient in whom clinical coronary artery disease developed within 4 years after entry testing. Thus, the treadmill ECG provided prognostic information not available from the history and physical examination results. Importantly, prognostic information was limited to the first 4 years of follow-up (sensitivity 43%, specificity 77% at 8 years) suggesting the need for serial testing.

In the only study to date to directly compare the utility of diagnostic tests in diabetic versus normal populations, we carried out a retrospective analysis of 1282 male patients without previous MI who underwent exercise testing and coronary angiography [46]. We found similar values for sensitivity and specificity in the diabetic patients as in the non-diabetic controls 47% (CI 41–58) and 81% (CI 68–89) versus 52% (CI 48–56) and 80% (CI 76–83) – a finding which strongly suggests that the exercise test remains a useful tool in the diabetic population.

Nuclear techniques

Isotopes such as thallium-201 or technetium-99m can be used to provide information on cardiac function. Perfusion imaging is aimed at assessing regional blood flow by comparing the relative distribution of isotope at rest and under conditions of stress. Stress is provided either by exercise or by pharmacological tools such as inotropes (dobutamine) or vasodilators (adenosine or dipyridamole). The isotope is injected a peak exercise and the image captured with a gamma-camera. Rest images are usually achieved several hours later, and the images compared to identify perfusion defects which are either 'fixed' (e.g. the scar of an old MI) or 'reversible' (ischemic disease). For many years, thallium has been the agent of choice, but more recently centres have been using technetium-99m-labeled compounds such as sestamibi, which offer higher resolution for lower radiation dose. Single photon emission computed tomography (SPECT) is a technique that employs a gamma-camera head rotating around the patient to provide three-dimensional images.

Holley *et al*. [47] reported that the predictive value of nuclear perfusion scans for significant coronary artery disease and peri-operative cardiac events in diabetic patients with end-stage renal disease was relatively low. Similarly, Koistinen *et al*. [48] found the accuracy of an abnormal exercise electrocardiogram to be better than that of nuclear perfusion scanning for detecting asymptomatic coronary artery disease in diabetic patients mostly due to a high false-positive rate of thallium imaging. However, Giri *et al*. [49] assessed the value of stress SPECT perfusion imaging for risk stratification in diabetic patients and showed that when cardiac survival was adjusted for clinical variables and SPECT the difference between diabetic patients and non-diabetic controls disappeared. This suggests that the risk associated with diabetes was 'subsumed' within the SPECT stratification. In contrast, however, the 2-year event rate in diabetic patients with normal SPECT was higher than the non-diabetic controls with normal SPECT, suggesting that this effect does not extend to those with negative tests [50]. Finally, it should be noted that this study does not inform the issue of screening: patients were included on the basis of suspected or established coronary artery disease, with the presence or absence of symptoms and duration of disease not reported.

Stress echocardiography

One of the most effective alternatives to the exercise treadmill test is stress echocardiography. It relies on the fact that ischemic myocardium moves less than non-ischemic myocardium. In this way, 'segmental defects' that point to the coronary disease pattern can be detected. However data establishing the technique firmly as a diagnostic test in the diabetic population have only recently been published. Elhendy *et al*. [51] carried out exercise echocardiography in 563 diabetic patients who were followed up over 5 years. They showed that exercise echocardiography provided information on risk incremental to that provided by clinical and exercise test variables. Specifically, a multivariate model showed that a prior history of MI, treadmill exercise capacity, ejection fraction, and the percentage of ischemic segments were most predictive of cardiac event risk. Furthermore, patients with multi-vessel disease distribution had a 33% 5-year risk of cardiac death or non-fatal MI. One drawback of this study, however, is that the authors did not account for duration of disease so it is difficult to draw specific conclusions about the place of exercise echocardiography in screening diabetic populations.

Electron beam computed tomography

Electron beam computed tomography (EBCT) is a fast radiographic technique that can make a quantitative measurement of coronary artery calcification [52]. The significance of the resulting 'plaque burden' measurements remains controversial [53]. Mielke *et al*. [54] carried out EBCT in 3389 coronary artery disease patients and found that coronary artery calcium scores were higher in males and those with diabetes. However, a clear association between coronary artery calcium and risk in the diabetic patient has not been shown. In addition, issues of cost, radiation exposure, and the relation between coronary calcium and plaque stability will need to be resolved before widespread adoption of this technique can be recommended.

Cardiovascular magnetic resonance imaging

Most cardiologists agree that the future of non-invasive imaging of the heart lies with magnetic resonance imaging (MRI). Although this technology is not yet widely available, it can fulfil many of the functions of traditional tests and in most cases improve on them [55]. Cardiac anatomy and morphology can be assessed with a high degree of spatial resolution using 'black blood' imaging. In cine mode (like two-dimensional echo), a significantly greater resolution than ultrasound can be achieved and good views imaged and processed in under 30 s. Left ventricular function including under exercise or pharmacological 'stress' can be assessed with a single breath hold and circumferential shortening calculated. Wall motion abnormalities can be assessed using 'tagging' techniques. Perfusion imaging can be carried out with a single breath hold and two R-R intervals. In fact, the only technique that is still some way from potential routine clinical application is MR angiography of the coronary vessels (larger vessel MR angiography has been possible for some time). However, as new technology moves the field forward, this is likely to come within reach, and with it the enticing prospect of cross-sectional imaging and plaque characterization.

Comparison of diagnostic tests

Since sensitivity and specificity are altered by the chosen cutpoint for normal/abnormal, the predictive accuracy is a convenient way to compare tests (Table 1). This represents the percentage of patients correctly classified. For instance, while the sensitivity and specificity for exercise testing and EBCT are nearly opposite, their predictive accuracy is similar. Altering their cutpoints by lowering the amount of ST-segment depression or raising the calcium score would result in similar sensitivities and specificities (although this assumes a disease prevalence of 50%). The general message from Table 1, however, is that while the newer technologies appear to have better diagnostic characteristics than the basic exercise test, this advantage does not bear comparison, in the general population at least, to methods incorporating other clinical information such as the exercise test scores. To date, there have been few studies adding the predictive power of clinical data to the newer tests in clinical scores.

Optimising the variables: exercise test scores

The application of multivariate analysis to clinical and exercise test variables has repeatedly been shown to improve the diagnostic characteristics of the exercise test. Although occasionally single variables are found to be highly predictive (May *et al*. [28] found that systolic blood pressure alone was highly predictive of silent ischemia in diabetic subjects), it is likely that, as with the non-diabetic population, consideration of clinical variables together with exercise test variables will improve the test characteristics in diabetic patients. A recent meta-analysis of 24 studies that considered exercise test and clinical variables to predict the presence of any angiographic disease summarized the results in over 6000 patients presenting with chest pain [56]. In fact, diabetes itself was found to be a good predictor in four of the 11 studies that considered it, out of the 24 diagnostic studies predicting the presence of any angiographic coronary disease. However, this variability serves to illustrate the limited portability of the equations derived to populations other than those in which they were developed. In addition, detailed information on the diagnosis, duration and treatment of diabetes was often lacking in these studies. Approaches to overcome these problems have been developed [57], but so far not widely applied to the diabetic population. In one study that did, Manske *et al*. developed a non-invasive screening algorithm from tests on 141 consecutive asymptomatic type 1 diabetic renal transplant candidates [58]. The final algorithm included smoking for five or more pack years, non-specific ST-T wave changes and diabetes duration 25 years or longer. This tool had a sensitivity of 97% and a negative predictive accuracy of 96%. These authors concluded that coronary angiography should be recommended for similar diabetic patients aged 45 years or older because of the high probability of disease.

Who to screen?

Whilst authors [59] and expert panels [2] have speculated as to the place of these techniques in screening asymptomatic diabetic patients for coronary disease, these suggestions are made on the basis of experience, rationality and the application of logical thought. There exists at present no clear evidence base from which to derive recommendations. The American Diabetes Association (ADA) consensus statement [60] recommends testing asymptomatic diabetic patients with two or more risk factors for coronary disease. Others [43] believe that the presence of one other major risk factor in addition to a history of diabetes longer than 5 years is sufficient for the rational diabetologist to consider a screening exercise stress test. Studies are presently underway [50] to address this lack of evidence but it will be some time before results are available.

Conclusions

In this paper we have provided an overview of the problems unique to the diagnosis of coronary disease in diabetic patients. Silent ischemia is common (up to 30% prevalence in some studies); it almost certainly relates to autonomic dysfunction and probably occurs more commonly in diabetic patients than the general population. Furthermore, it seems to be associated with similar or poorer prognosis than non-silent disease, providing a strong argument for screening asymptomatic individuals. Finally, relating to the choice of diagnostic test, few data are available specific to the diabetic population, but what there are suggests that the exercise stress test should remain the first choice. It is cheap, quick, safe, can be carried out without the presence of a cardiologist in the majority of cases, and has a predictive value in diabetic patients equal to that in the normal population. Furthermore, when combined with other clinical variables in scores, it outperforms much more expensive tests. However, in the many cases where exercise testing alone is not appropriate or sufficient, incremental prognostic data can be gathered from SPECT perfusion imaging and stress echocardiography. In particular, the latter technique can provide information on left ventricular dysfunction. In the final analysis, we concur with other authors [43] who believe that the presence of one other major risk factor in addition to a history of diabetes longer than 5 years is sufficient for the rational diabetologist to consider a screening exercise stress test. For our part, we are left in no doubt: diabetes is a cardiovascular disease.

Appendix

ADA Position Statement on Diabetes and Exercise

The revised position statement was published in 1997 and stated the place of the standard exercise test in evaluating diabetic patients about to embark on a moderate to high intensity exercise program [61]. An exercise test was given a IIb indication as 'may be' helpful in high-risk individuals. High risk for underlying cardiovascular disease in diabetic patients without symptoms of cardiac disease was empirically associated with one of the following criteria:

- Age greater than 35 years
- Type 2 diabetes of greater than 10 years duration
- Type 1 diabetes of greater than 15 years duration
- Presence of any additional risk factor for coronary artery disease
- Presence of microvascular disease (retinopathy, nephropathy, proteinuria)
- Peripheral vascular disease
- Autonomic neuropathy.

In patients planning a low-level exercise program such as walking, physician judgement is to be used to decide who needs an exercise test.

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