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Diagnostic imaging

Non-invasive imaging of diabetic vascular disease

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Abstract

A high proportion of diabetic subjects are referred with atherosclerotic disease and higher risk for cardiovascular events. Rapid expansion of the use of non-invasive coronary and peripheral arteries imaging, facilitated by technological advances, have found diagnostic and prognostic roles in this population. This review, which includes important and actual works, guidelines, and algorithms on cardiovascular disease in the diabetic population, indicates mandatory screening for arterial disease in these patients in light of their appropriate management.
Key words: imaging, diabetes, stress myocardial perfusion, stress echocardiography, electron beam tomography, MR, CT, vascular ultrasound

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Introduction

The prognosis of patients with diabetes mellitus depends on the presence of vascular disease. Coronary artery disease (CAD) is the leading cause of death in people with diabetes mellitus. It has been reported that the 7-year cardiovascular mortality rate among patients with type 2 diabetes without a prior history of myocardial infarction is as high as that in non-diabetic patients with previous infarction [1]. Since the risk for complications due to CAD can be modified by appropriate interventions, early detection is important [2]. Because of this high risk of CAD and the poor outcome among asymptomatic patients with type 2 diabetes, clinicians should use aggressive strategies to diagnose CAD to reduce or prevent cardiovascular morbidity and mortality in these patients.

Several factors are known to differentiate CAD in patients with diabetes from CAD in non-diabetic patients. These factors may provide clues as to the differences in prognosis for patients with diabetes, as well as suggest the limitations of available testing methods. For example, although atherosclerotic plaque appears to be morphologically similar among patients with or without diabetes, pathologic studies have demonstrated that coronary arteries in patients with diabetes and CAD show diffuse disease, in contrast to the more localized involvement often seen in the absence of diabetes [4]. Symptoms of myocardial ischaemia are often absent or atypical in diabetic patients, and CAD is frequently detected at an advanced stage, characterized by extensive atherosclerotic obstructive coronary disease. Diabetes also is associated with generalized endothelial dysfunction and small-vessel abnormalities, in addition to the larger-vessel abnormalities seen in non-diabetic patients with CAD [4, 5].

There are two points of view for the interplay of peripheral arterial disease (PAD) and cerebrovascular disease (CVD) with diabetes: The higher prevalence of PAD and CVD presented in the diabetic population than in the general population, and secondly that peripheral atherosclerosis is a marker of general atherosclerosis in these patients [6]. Peripheral arterial disease occurs in diabetics with a 3-fold higher risk than in the general population. Prognosis of patients with PAD and diabetes depends on future cardiovascular events, which are two to four times more frequent than in the general population [7–8].

Diabetes is also one of the most important risk factors for development of cerebrovascular disease, defined as ischaemic stroke or asymptomatic carotid stenosis [9, 10]. The relative risk for stroke in diabetic subjects is 2.1–5.8 [6]. Development of carotid atherosclerosis in diabetic subjects is related to glycaemia and plasma cholesterol LDL and non-HDL level [11–14].

The clinical role of imaging atherosclerosis

Technological advances have facilitated a rapid expansion in the use of non-invasive coronary and peripheral arteries imaging. There are now numerous options offering enhanced image quality and better anatomic definition, which were previously unavailable without catheterization. These less invasive imaging procedures are becoming important gatekeepers, helping to select patients for catheterization in anticipation of treatment.

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Various non-invasive tests are available to identify patients at high risk of atherosclerotic disease, including myocardial perfusion scintigraphy, stress echocardiography, calcium scanning, cardiac MRI, multi-sliced MSCT angiography, and vascular ultrasound.

Stress myocardial perfusion imaging with gated SPECT

The use of standard exercise ECG testing in patients with diabetes continues to be an area of concern and controversy. In addition to having decreased exercise capacity, diabetic patients often experience no chest pain during exercise, and the standard exercise ECG may be less reliable for detecting significant CAD in diabetic patients [15, 16]. Painless ST-segment depression during treadmill exercise is common in diabetic persons, and the diagnostic specificity of ST depression is often reduced in these patients [17].

Given the prevalence of CAD in patients with type 2 diabetes, the American Diabetes Association (ADA) recommends performing a cardiovascular risk assessment at least yearly [18]. In addition, the ADA recommends exercise stress testing in all asymptomatic patients with diabetes. The optimal frequency of stress testing is unknown although it has been suggested that stress testing should be considered every 3 to 5 years for asymptomatic patients with no new risk factors [19]. For patients with multiple or new risk factors, testing should be increased to every 1 to 2 years. Exercise ECG testing has a relatively high specificity and sensitivity (68% and 77%, respectively) [3], but often diabetic patients cannot perform an exercise test because of complications such as leg ischaemia or lower cardiorespiratory capacity. In general, exercise-ECG may not be ideal due to the lower accuracy for assessment of ischaemia and the inability of a substantial amount of patients with diabetes to perform an exercise test. The lower accuracy of exercise-ECG may be, in part, related to the ischaemic cascade, in which ECG abnormalities occur late in the cascade.

The combination of imaging and stress testing may thus be preferred for assessment of myocardial ischaemia. Imaging allows visualization of induction of perfusion (using nuclear imaging) or systolic wall motion abnormalities (mainly echocardiography, but magnetic resonance imaging can also be used), both sensitive markers of ischaemia. In addition, the imaging studies can be performed in combination with pharmacological stress, rather than physical exercise, when needed. A large body of evidence attests to the high diagnostic yield of stress myocardial perfusion imaging and its important incremental prognostic value over both clinical and angiographic variables for the prediction of major acute coronary events [19, 20]. The degree and extent of myocardial perfusion abnormalities observed in stress myocardial perfusion abnormalities are related directly to outcome. The greater the myocardial perfusion abnormality, the greater the likelihood of future cardiac events. On the other hand, unequivocally normal stress myocardial perfusion imaging is associated with an excellent outcome and a cardiac event rate of $<$ 1% per year [17, 21]. Several investigators have reported that single-photon emission computed tomography (SPECT) myocardial perfusion imaging had similar prognostic value in patients with diabetes mellitus.

Giri et al. [13] evaluated stress SPECT myocardial perfusion imaging for risk stratification of patients with diabetes mellitus. In this multicentre, database analysis involving a large number of subjects, patients with diabetes mellitus had a significantly higher cardiac event rate (death and myocardial infarction) than that of the non-diabetic patient cohort. When adjustment was made for clinical variables and SPECT myocardial perfusion imaging results, however, cardiac survival was comparable, indicating that myocardial perfusion imaging prognostic categorization supersedes the adverse predictive value of diabetes mellitus as a univariable parameter. Interestingly, women had a worse outcome for any given extent of myocardial perfusion abnormality than men did. Of substantial clinical interest was the observation that after the index study, patients with diabetes mellitus and normal stress SPECT images had a significantly higher two-year cardiac event rate than that of patients without diabetes. This prognostic finding is in marked contrast to the experience in the non-diabetic population, in which the association of normal myocardial perfusion imaging and excellent outcome has been demonstrated repeatedly [19, 23]. Defining the factors responsible for this altered prognostic value of normal myocardial perfusion imaging in diabetic patients will require further study. However, patients with diabetes mellitus and normal stress images may require more frequent follow-up testing. Current radionuclide imaging guidelines have reported the average sensitivities and specificities of exercise and vasodilator stress perfusion single-photon emission computed tomography (SPECT) for detecting angiographically significant CAD (Table 1). Generally uncorrected for referral bias, the sensitivities average 87% for exercise and 89% for vasodilator stress, and the specificities average 73% for exercise and 75% for vasodilator stress [22, 24].

When to do cardiac screening with myocardial perfusion imaging in patients with diabetes

The ADA recommends annual evaluation of patients with diabetes. Exercise electrocardiography (ECG) is recommended as the initial screening tool to help identify patients who would be considered at higher-than-average risk of cardiac events [35]. Candidates for myocardial perfusion imaging include patients with:

- typical or atypical signs or symptoms of CAD;
- an abnormal resting ECG;
- peripheral or carotid arterial disease;
- age over 35, a sedentary lifestyle, and plans to initiate an exercise program;
- two or more of the following, in addition to diabetes:
  a) elevated total and low-density cholesterol or low high-density cholesterol; elevated blood pressure; smoking; family history of premature CAD or
  b) positive microalbuminuria or macroalbuminuria;
- inadequate exercise electrocardiographic results;
- no symptoms but mildly or moderately positive exercise electrocardiograms (ECGs);
- clear or suggestive evidence of ischaemia or infarction on baseline ECG;
- mild angina and normal or near-normal ECGs.

For patients at low risk of cardiovascular events, a standard treadmill exercise test is often chosen. However, if a diabetic patient has typical angina or Q waves on a resting ECG, myocardial perfusion imaging should be performed to assess ventricular function and obtain quantitative information on the extent of the perfusion abnormality [2].

Table 1. Diagnostic accuracy of imaging tests. Reprinted (with permission) from [22]

	General population		Diabetic patients	
	Sensitivity	Specificity	Sensitivity	Specificity
Functional imaging [ref.]				
Nuclear imaging [11–14]	86	74	80–97	56–88
Stress echocardiography [15–18]	71–84	82–93	81–92	54–88
Contrast echocardiography [21, 22]	89	63	89	52
First-pass perfusion MRI [21]	84	85	NA	NA
Stress cine MRI [21]	89	84	NA	NA
Anatomical imaging [ref.]				
CAC score	NA	NA	NA	NA
MRI angiography [27]	72	86	NA	NA
MSCT angiography [28, 29]	91	96	95	95
EBCT angiography [30]	87	91	NA	NA

In non-diabetic patients, the low event rate in the presence of a normal study is maintained for years, but in diabetic patients, the so-called warranty period of a normal study is limited to 2–3 years, indicating the rapid progression of coronary artery disease in these patients. For example, Elhendy et al. [5] demonstrated that the event rate in diabetic patients with a normal exercise echocardiogram increased from 0% in the first year to 1.8% at 3-year follow-up and 7.6% at 5-year follow-up.

Still, the available data reveal a high incidence of patients with silent ischaemia among asymptomatic patients with type 2 diabetes. For example, in the Detection of Silent Myocardial Ischaemia in Asymptomatic Diabetics (DIAD) study, 22% of patients exhibited evidence of silent myocardial ischaemia on nuclear myocardial perfusion imaging [26]. Of interest, 41% of all abnormal SPECT studies occurred in patients with less than two risk factors. Moreover, multivariate analysis demonstrated that only autonomic dysfunction was predictive of an abnormal SPECT study. The precise incidence of silent ischaemia is not clear; Rajagopalan et al. [23] recently reported that 58% of asymptomatic patients with type 2 diabetes had an abnormal SPECT study, whereas Zellweger et al. [19] noted that 42% of asymptomatic diabetic patients had an abnormal SPECT study. However, these observations demonstrate that silent ischaemia is common among patients with type 2 diabetes, and screening may be indicated. Whether SPECT imaging should be the first line test, however, is still unclear.

Anand et al. [17] proposed an algorithm for the screening of patients with type 2 diabetes for coronary artery disease. The authors evaluated asymptomatic patients with type 2 diabetes using electron beam computed tomography (EBCT). This imaging technique allows visualization of atherosclerosis (coronary artery calcium) rather than ischaemia, and may thus permit identification of coronary artery disease at an early stage. Nuclear myocardial perfusion imaging was performed in patients with calcium score > 100 Agatston units, i.e. 127 (25%) underwent gated exercise sestamibi SPECT. For comparison, 53 randomly selected patients with a calcium score of 100 also underwent SPECT. None of the patients with a calcium score of 10 had abnormalities on SPECT. The incidence of abnormal SPECT studies increased in parallel with the calcium score, from 18.4% in patients with calcium score between 11 and 100 to 71.4% in patients with calcium score > 1000. These observations suggest that sequential use of EBCT and SPECT may optimize screening of asymptomatic diabetic patients, and EBCT may be used as a gatekeeper for SPECT. This proposal is further strengthened by the prognostic data also provided in the study by Anand et al. During a mean follow-up of 18 ± 5 months, no events occurred in the patients with calcium score ≤ 10, whereas the majority (82%) of events occurred in patients with calcium score > 400. Importantly, on multivariate analysis, the calcium score and the extent of SPECT perfusion abnormalities were the only predictors of future events. On the basis of this stepwise approach, patients with atherosclerosis on EBCT but without ischaemia may be referred for risk factor modification, aggressive medical therapy, and careful monitoring. Conversely, patients with atherosclerosis and ischaemia may be referred for invasive coronary angiography with intervention if required.

The future in non-invasive imaging is very bright. The latest application of fusion imaging (SPECT/CT and PET/CT hybrid systems) allows simultaneous assessment of coronary anatomy and physiological significance of the CAD. This will further select the patients who need invasive treatment, with previous knowledge of coronary anatomy and haemodynamic significance of stenosis, and will allow target vessel revascularization.

Stress echocardiography

Stress echocardiographic testing has been shown to provide incremental prognostic information in the general population. Some studies have demonstrated an incremental value of pharmacological and exercise stress echocardiography on the prognosis of diabetic persons, specifically [27, 28]. Diabetic patients had a significantly higher incidence of cardiac events than did patients without diabetes [22]. There were more nonfatal myocardial infarctions in the diabetic group and a trend toward a higher proportion of hard events, including cardiac death. The rate of hard events annually was 2.7% in non-diabetic and

6.0% in diabetic patients. Compared with non-diabetic patients, patients with diabetes who have negative stress echocardiograms appear to remain at greater risk for cardiac events, possibly because of a higher prevalence of established coronary disease in patients with diabetes. On the basis of limited data, it appears that exercise echocardiography offers prognostic information in patients with diabetes, but even with negative studies, patients with diabetes are at higher risk for cardiac events than patients without diabetes. There is limited outcome data available that show any benefit of testing in the asymptomatic population, and thus, routine use of this test cannot be widely recommended [29]. Based on our own findings, routine screening is recommended for patients in whom the duration of type 2 diabetes is > 10 years or even less when more than one cardiovascular risk factor is present [30].

Despite the widespread use and reported accuracy of stress echocardiography, it is technically challenging, and reproducibility is still somewhat limited due to high inter-observer variability. Standard echocardiographic examinations may be suboptimal in quality and frequently do not yield sufficient diagnostic information. In diabetic patients, many of whom are overweight, the increased weight contributes to a poor echocardiographic image. In addition, many diabetic patients cannot exercise adequately because of increased weight and neuropathic complications. Conflicting results regarding the sensitivity (in the range 60-80%) and specificity (44-58%) of stress echocardiography for predicting clinical events in diabetic patients were reported by different studies, although these differences did not reach statistical significance.22,31 Bax et al. [22] in a review study reported the specificity of stress echocardiography in diabetic patients to be lower than that of nuclear perfusion imaging.

However, stress echo offers the advantage of easy portability, lower cost, and no radiation exposure compared with nuclear stress testing, and it has therefore gained substantial popularity.

Electron beam tomography measures of coronary calcium

Electron-beam CT can be used to measure calcification of coronary arteries, an early marker for CAD [20]. This technique has substantial potential for risk assessment [21]. However, although it can detect the presence of atherosclerosis, it cannot measure the severity of obstruction. In addition, a low calcium score does not rule out CAD. Because this technique has low specificity, the American College of Cardiology does not recommend its routine use in the diagnosis of CAD. Electron-beam computed tomography (EBCT) can noninvasively and accurately detect coronary calcification, which is a predictor of ischaemic heart disease [3]. Plaque calcifications usually precede luminal narrowing and the onset of angina symptoms. The sensitivity and specificity of EBCT for the detection of stenosis have been reported to be > 90% and > 50%, respectively [4].

In type 2 diabetic patients, Schurgin et al. [32] showed that asymptomatic diabetic patients had a significant increase in the prevalence of coronary calcification score compared with matched non-diabetic control groups. However, it is not known whether coronary calcifications in diabetic patients are associated with the presence of significant coronary stenoses. Rumberger et al. [33] reported that a coronary calcium score (CCS) of 80 had a sensitivity of 84% and a specificity of 84%. These data are in keeping with our finding that a CCS of 90 was associated with a sensitivity of 75% and a specificity of 75% for the detection of significant stenoses in diabetic patients.

Consequently, coronary calcium is considered an accurate marker of atherosclerosis. Though often misrepresented, the main purpose of calcium screening is not to identify patients with obstructive CAD but to detect vessel wall atherosclerosis. In fact, identifying non-obstructive plaque may be as important as assessing stenosis severity since many acute coronary events occur on the basis of non-obstructive disease in type 2 diabetes. Mielke et al. [34] studied a large cohort of patients suffering from type 2 diabetes and showed that these patients tend to harbour larger amounts of CAC than non-diabetic patients of similar age and with a similar risk-factor profile. Moreover, the amount of CAC was similar to that of patients with established CAD but without diabetes. Similarly, Khaleeli et al. [35] showed that asymptomatic diabetic patients present the same prevalence of CAC as non-diabetic individuals symptomatic for CAD. Furthermore, both studies showed that diabetic women harbour as much CAC as diabetic men, confirming the clinical evidence that diabetes negates the well-known advantage of women over men in prevalence and extent of atherosclerosis. Furthermore, the calcium imaging data are supportive of the well-known clinical data showing that an asymptomatic diabetic patient presents the same cardiovascular risk as a patient with established CAD but without diabetes [22].

Recently Raggi et al. [16] published a report of asymptomatic individuals, with a large type 2 diabetic subgroup, followed for an average of 5 years after having been referred by a primary care physician for CAC screening. The risk of all-cause mortality was higher in diabetic patients than non-diabetic subjects for any degree of calcification, and the risk increased as the calcium score increased.

Coronary calcium to assess coronary plaque burden and future events

Coronary artery calcium is intimately associated with mural atheromatous plaque and is pathognomonic of atherosclerosis. Clinical and histopathological studies confirm the close correlation between the extent of coronary artery calcification (CAC) and the burden of atherosclerotic coronary disease. The total area and volume of coronary artery calcification, determined by EBCT, correlates in a linear fashion with the total area of coronary artery plaque on a segmental basis [33]. The EBCT coronary calcium score may not always predict the existence of significant luminal narrowing, but the sensitivity of EBCT to detect obstructive luminal disease increases with higher plaque burden (especially with an Agatston score of 400 or more) [34]. A negative EBCT test (absence of coronary calcium) makes the presence of atherosclerotic plaque, including unstable plaque, very unlikely — this usually occurs in people with angiographically normal coronary arteries and is consistent with low risk of a cardiovascular event in the next two to five years [37]. The extent of CAC predicts the risk of future hard cardiovascular events in symptomatic patients and has a better prognostic value compared to coronary angiography [38]. Furthermore, there is a direct relationship between increasing calcium scores and the occurrence of subsequent cardiac events. Several prospective randomised trials have established the predictive value of CAC for future coronary events in asymptomatic individuals with varying risk factor profiles. A high calcium score (≥ 1,000) on a screening EBCT in an asymptomatic person predicted a very high risk of hard cardiac events (death and MI) in the short term [39]. However, none of the 98 patients in the above study underwent either non-invasive or invasive testing as a direct consequence of their EBCT scores. In the current climate it is unlikely that patients with such extensive plaque burden would be untreated, and it will be interesting to see whether EBCT could be used to monitor therapeutic success.

It is well known that patients with severe coronary stenoses can often be asymptomatic. In diabetic patients without cardiac symptoms or signs but with other cardiovascular risk factors, silent myocardial ischaemia has been found in 10–30% of cases [31].

In a recent study of type 2 diabetic patients, Rutter et al. [31] found that silent myocardial ischaemia was the strongest independent predictor of future CHD events. In a comparative study Schurgin et al. [32] showed that patients with type 2 diabetes have a significantly higher prevalence of CAC scores > 400, consistent with a greater atherosclerotic plaque burden compared with randomly selected and matched non-diabetic control groups. This leads us to an important question: Who should be screened by EBCT?

After evaluating the existing literature on EBCT coronary calcium imaging in 2000, The American College of Cardiology/American Heart Association joint task force on clinical expert consensus documents concluded that EBCT has a role in selected asymptomatic patients in whom standard risk assessment is considered insufficient [15, 37]. Since age appears to be a surrogate marker for the total coronary atherosclerotic plaque burden, it has also been suggested that the coronary calcium score should replace age as a risk factor in Framingham scoring for CAD risk assessment. EBCT coronary calcium imaging plays an important role in the accurate risk stratification of asymptomatic patients with one or more conventional risk factors for coronary disease, in whom clinical decision making regarding the need for medical intervention can often be uncertain. Currently the best example of this strategy is with regard to the decision of whether to institute cholesterol-lowering and antiplatelet drug therapy.

Magnetic resonance imaging

High-resolution magnetic resonance (MR) is a non-invasive imaging technique with excellent soft-tissue contrast that differentiates plaque components on the basis of biophysical and biochemical parameters. Further improvement in external coils and the use of contrast agents that enhance the different vessel wall components hold great promise and may make MR suitable for clinical use in atherosclerotic plaque diagnosis and in monitoring

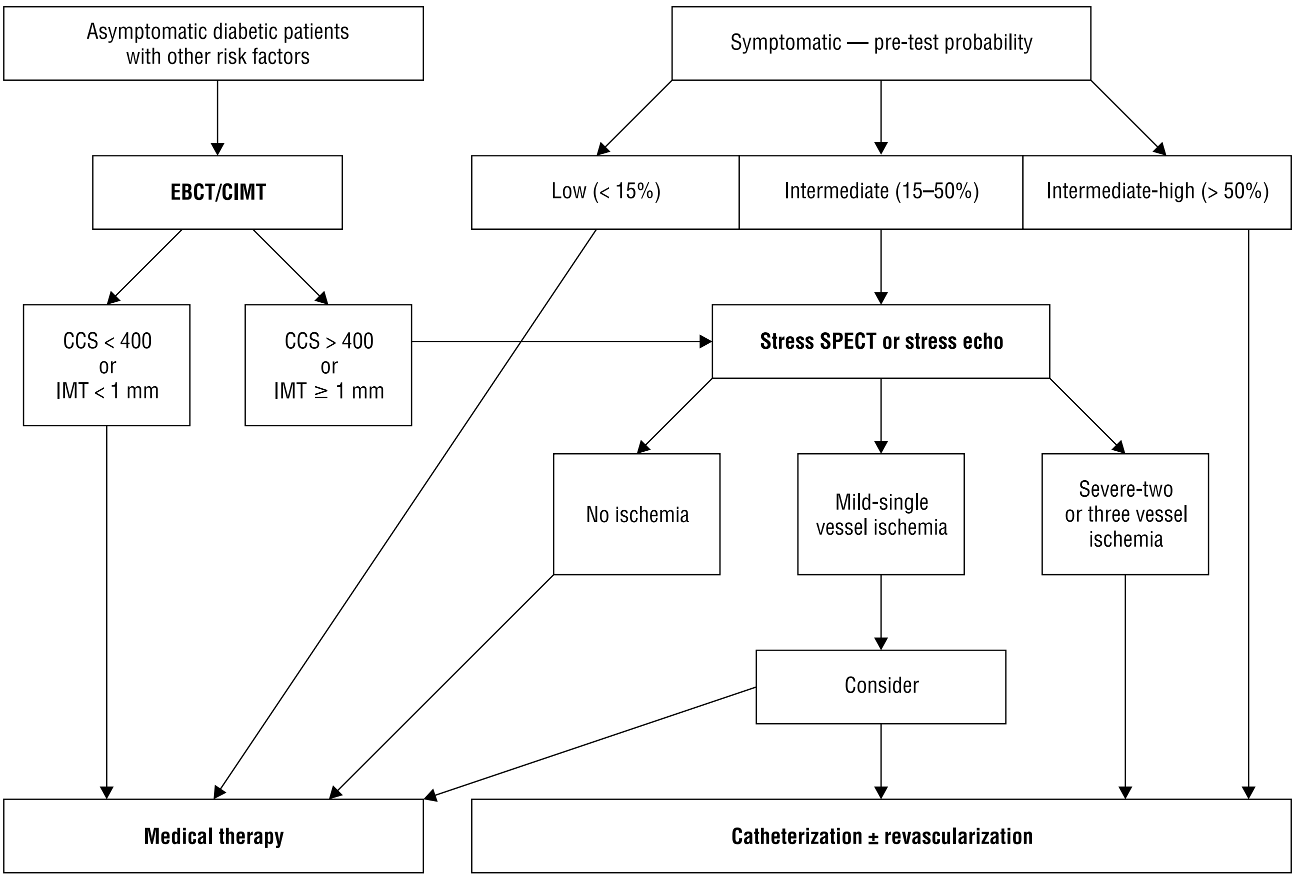

Figure 1. Algorithm for diagnosis and treatment of CAD in diabetic patients. Reprinted (with permission) from [16].

therapeutic efficacy [40]. Future work in coronary MR plaque imaging will certainly aim at the identification of the different plaque components, with increasing focus on persons with diabetes. This may enable identification of vulnerable plaques before they rupture and may provide a way to target pharmacological intervention to reduce or prevent coronary disease. The assessment of atherosclerotic plaques by imaging techniques may prove valuable for the identification of vulnerable plaques. In vivo high-resolution multicontrast MR holds promise for noninvasively imaging vulnerable plaques and characterizing the different components in all arteries, including the coronary arteries. MR stress testing provides important incremental information about clinical risk factors and resting wall motion abnormalities in a high risk patients, including those with diabetes [41].

Magnetic resonance angiography in peripheral arterial disease

Magnetic resonance angiography (MRA) is useful in the diagnosis of anatomic lesions and the grade of peripheral artery stenosis after a functional study with indexes is conducted. Selection of the suitability of a lesion for percutaneous revascularization is a second indication for its usage. Both indications are applied in peripheral arterial disease subjects including diabetic subgroups with IA levels of evidence according to AHA/ACC Guidelines [42]. Magnetic resonance angiography for extremities should be performed with gadolinium enhancement. Andreisek et al. [43] presented time-resolved imaging of contrast kinetics MR angiography of the distal calf and pedal vessels as superior to standard MR angiography regarding the number of diagnostic segments and assessment of the degree of luminal narrowing in diabetics. Therefore, MRA should be part of the diagnostic algorithm for patients in whom pedal bypass grafting is a therapeutic option [44]. MR angiography of intracranial arteries has been recognized as useful in patients with intracranial steno-occlusive lesions and either diabetes or the presence of risk factors. These patients could be followed up by serial MR angiography of intracranial arteries [45].

Multi-sliced MSCT angiography

In the last 10 years computed tomography (CT) has progressed from single-slice scanners to the current generation of 64-slice machines that can image the whole heart in seconds with sub-millimetre resolution. Consequently, multislice computed tomography (MSCT) scanning is rapidly gaining acceptance as an alternative to conventional X-ray coronary angiography. 64–slice MSCT angiography can quickly and accurately detect coronary stenosis in a way that is convenient to patients. Diabetic patients with borderline myocardial perfusion imaging findings of moderate ischaemia should be referred for MSCT angiography. Patients with severe, extensive ischaemia are directed to invasive coronary angiography. There are currently no published guidelines for the clinical application of CT coronary angiography. Patients who have chest pain, but who are of low-to-moderate risk or have equivocal stress tests are ideal candidates for CT coronary angiography, as are patients who are asymptomatic but who are a very high risk for early or severe cardiovascular disease. For particularly anxious patients with atypical chest pain, the combination of a low-risk stress test and a negative CT coronary angiogram is a powerful tool for reassurance. Often more importantly, the ability to demonstrate mild coronary atherosclerosis can lead to lifestyle and diet changes, as well as encouraging compliance with medical therapy. There are situations in which CT coronary angiography is useful after an invasive catheterisation has already been performed. MSCT is particularly well suited for defining the exact origin and course of anomalous coronary arteries identified by conventional coronary angiography. Like intravascular ultrasound, MSCT is able to demonstrate pathology in the wall of the artery, and not just define obstruction of the lumen. In this manner, a coronary angiogram can often give a more total view of coronary pathology, including evaluation of the lumen, the amount of soft, fatty plaque, and calcified plaque burden in the coronary vasculature. Romeo et al. [46] in their study calculated the value of multislice computed tomography for early detection of significant coronary artery disease (CAD) in high-risk asymptomatic subjects. Selective coronary angiography confirmed the results of multislice computed tomography in 99% of asymptomatic subjects with more than one major risk factor (hypertension, diabetes, hypercholesterolaemia, family history, or smoking) and an inconclusive or unfeasible noninvasive stress test result (stress electrocardiography, echocardiography, or nuclear scintigraphy) [47]. Multislice computed tomography displayed single-vessel CAD in 16% of patients, 2-vessel CAD in 7%, and 3-vessel CAD in 4%. Sensitivity and specificity of MSCT coronary angiography were 100% and 98%, respectively, with a positive predictive value of 95% and a negative predictive value of 100%. MSCT is also very well suited to evaluating the patency of coronary bypass grafts, and in some cases may obviate the need for stress testing in patients who have undergone bypass surgery.

Multi-sliced CT angiography in peripheral arterial disease (PAD)

Multi-sliced ct angiography (MSCT) angiography has not been established as a routine screening method for detection of PAD in diabetics. It could be used for the detection of anatomical lesions in leg ischaemia patients when revascularization is indicated and in those with conflicted reports of vascular duplex ultrasound. It is considered as a substitute for MRA for patients with contraindications for MRA [48].

Vascular ultrasound

Carotid ultrasound examination is indicated in the presence of stroke [49]. Ultrasound capabilities facilitate decision making regarding the appropriateness of medical therapy or surgical intervention in these individuals. Significant grade ($> 60\%$) carotid stenosis in diabetic patients needs elective endarterectomy or carotid stenting as the preferable method when high risk exists. Patients with stroke caused by non-significant carotid artery disease should be aggressively medically treated [6].

General screening for carotid artery disease is not recommended in most guidelines regarding diabetes. This is due to the low prevalence (4.5%) of significant carotid stenosis in asymptomatic subjects and to the costs of equipment and training [50].

Focused carotid screening in diabetics is recommended where cervical bruits exist and in subjects with symptomatic or asymptomatic PAD, defined by ankle-brachial index. Since the prevalence of diabetes increases constantly, Duval et al. [51] suggested updating the criteria for the selection of diabetics for carotid ultrasound; it could be also recommended for diabetic patients with coronary disease, all diabetic patients above 60 years of age, smokers, hypertensive with hypercholesterolaemia, and all type 2 diabetic patients with renal failure and long duration ill-controlled diabetes.

Nowadays there is no doubt that carotid intima media thickness can predict total cardiovascular events [52]. Carotid intima media thickness reflects the cumulative effect of risk factor exposure, and it is obvious that it can predict future risk. Carotid intima media thickness measurement may contribute to elucidating the effect of intervention on the rate of change in relation to the levels of various risk factors [53]. Carotid intima media thickness has been shown to have progressed significantly more in diabetic patients who received standard therapy than in those with intensive therapy.

Some recent studies show carotid plaque as a superior predictor of underlying CAD and future events than intima media thickness [54, 55]. All these studies include large subgroups of diabetics. Particularly for the diabetic population, Lee and Matsumoto independently presented an association of increased carotid intima media thickness and plaque with acute ischaemic stroke in type 2 diabetic patients [56]. The prevalence of carotid artery disease in a mean of plaque presence in diabetics is over 50%. Advanced carotid atherosclerosis is closely related with glycaemia, the lipid profiles of these patients, and responses to the patient's own risk factor burden [57–58].

Ultrasound measurement of progression of carotid atherosclerosis, plaque area, and volume (with using 3D-acquision for the last one) have been found to be closely linked with type 2 diabetes and vascular events in the general population [59]. Perhaps the application of this method has future possibilities and additional clinical usefulness in risk stratification of these patients.

Duplex ultrasound of the leg arteries is useful to diagnose the anatomic location and degree of stenosis of peripheral arterial disease and to provide surveillance following femoral-popliteal bypass and endovascular intervention. In all of these cases, continuous Doppler with index measurement is the first method of choice [48]. Few studies have described femoral artery intima media thickness as a prognostic parameter of type 2 diabetic patients, but its use as not as robust as carotid intima media thickness has to be.

Conclusions

The number of patients with type 2 diabetes will increase dramatically over the next few years. The preclinical diagnosis of coronary artery disease is effective in reducing the risk of cardiac events in subjects with diabetes mellitus who are at high cardiovascular risk. Management guidelines suggest non-invasive imaging techniques, such as nuclear myocardial perfusion imaging and stress echocardiography, for the detection of coronary artery disease in patients with symptoms of coronary artery disease. Although a substantial amount of patients may have silent ischaemia, not all patients may benefit from imaging to detect ischaemia. A stepwise screening with assessment of atherosclerosis by EBCT, followed by SPECT if needed, may allow optimal risk stratification of asymptomatic diabetes. Carotid intima media thickness has also been defined as a useful tool in risk stratification algorithm of diabetics. Screening for peripheral arterial disease and carotid artery disease should be mandatory for diabetic subjects, not only as a way of looking for the polyvascular disease, but also as a way of looking into the diabetic heart.

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