ABSTRACT

Introduction: Erectile dysfunction (ED) can precede coronary artery disease. In addition, silent myocardial ischemia (SMI) is more common in diabetic patients and is a strong predictor of cardiac events and death.

Aim: To evaluate the presence of SMI in patients with diabetes and ED using multidetector computed tomographic coronary angiography (MDCT-CA).

Methods: This study evaluated patients with diabetes and ED without any history of cardiac symptoms or signs. Erectile function was evaluated with the Sexual Health Inventory for Men score, erection hardness score (EHS), and maximal penile circumferential change by an erectometer. MDCT-CA was used for the detection of coronary artery stenosis.

Main Outcome Measures: Sexual Health Inventory for Men score, EHS, maximal penile circumferential change, and coronary artery stenosis by MDCT-CA.

Results: Of 20 patients (mean age = 61.45 ± 10.7 years), MDCT-CA showed coronary artery stenosis in 13 (65%) in the form of one-vessel disease (n = 6, 30%), two-vessel disease (n = 2, 10%), and three-vessel disease (n = 5, 25%). Fifty percent of patients showed at least 50% vessel lumen obstruction of the left anterior descending coronary artery, which was the most commonly affected vessel (55%). Fifteen percent (3 of 20) of patients had greater than 90% stenosis, and two of them underwent an immediate coronary angioplasty with stenting to prevent myocardial infarction. Maximum coronary artery stenosis was positively correlated with age (P = 0.016, r = 0.529) and negatively correlated with EHS (P = .046, r = −0.449). Multivariate regression analysis using age and EHS showed that age was the only independent predictor of SMI (P = .04).

Conclusion: MDCT-CA can be a useful tool to identify SMI in diabetic patients with ED, especially in those of advanced age and/or with severe ED.

Key Words: Diabetic Erectile Dysfunction; Silent Myocardial Ischemia; Multidetector Computed Tomographic Coronary Angiography

INTRODUCTION

Diabetes mellitus is a major public health problem around the world. It is estimated that the numbers of adults with diabetes will increase by 69% in developing countries and by 20% in developed countries from 2010 through 2030.1 Most patients with diabetes (90–95%) have type 2 diabetes mellitus.2 The death rate of diabetic adults is two to four times higher than for non-diabetic adults,2 with cardiovascular disease (CVD) being the commonest cause of death.3 The chronic hyperglycemia of diabetes is associated with macrovascular complications, including coronary artery disease (CAD), and microvascular complications that contribute to the pathogenesis of erectile
dysfunction (ED). A recent systematic review has interpreted the link between CAD and ED as an interaction of several factors, including cardiovascular risk factors, androgens, and chronic inflammation, which can lead to endothelial dysfunction and atherosclerosis, suggesting ED and CAD might be two different presentations of the same systemic disease.

The prevalence of ED in diabetic patients varies from 35% to 90%, with risk factors such as age, diabetes duration, glycemic control, sedentary lifestyle, smoking, and associated comorbidities. A meta-analysis has associated ED with increased risk of CVD events in diabetic patients. Even prediabetes identification in patients with ED has been associated with CVD predication. Penile color Doppler ultrasound has been recognized as a potential tool for predicting silent myocardial ischemia (SMI) in patients with ED.

Patients with SMI exhibit objective findings suggestive of myocardial infarction in the absence of angina or equivalent symptoms. Although the prevalence of SMI is highly variable depending on the targeted population, age, and diagnostic tools, diabetes is associated with a marked increase in SMI prevalence. Several studies have been conducted to screen for SMI in patients with diabetes using different tools with varying sensitivity and specificity, including electrocardiography, the ankle-brachial index, nuclear myocardial perfusion imaging studies, coronary artery calcium scoring using electron-beam computed tomography or multidetector computed tomography (MDCT), or a combination of such tests.

MDCT coronary angiography (MDCT-CA) has become a reliable non-invasive imaging modality with high specificity and sensitivity for the evaluation of CAD. MDCT-CA has been used to screen patients with asymptomatic diabetes for SMI, providing long-term prognostic value. Some studies have used MDCT-CA to screen for SMI in patients with ED. However, no previous studies have used MDCT-CA to screen patients with diabetes and ED.

AIM

This prospective study aimed to evaluate the presence of SMI in diabetic patients with ED using MDCT-CA.

METHODS

A prospective clinical study was conducted in diabetic men with ED seeking treatment at the Men’s Health Clinic at Juntendo University Hospital (Tokyo, Japan) from March 2014 through March 2015. The inclusion criteria for the study were the absence of current and/or previous cardiac symptoms and signs. The study design was approved by the ethical and scientific research committee of Juntendo University Hospital (number 14-065). The ethical principles of the Declaration of Helsinki were followed and an informed consent was obtained from all patients. Diagnosis of diabetes was based on criteria of the American Diabetes Association 2013 guidelines. Exclusion criteria included patients with cerebrovascular disease, congestive heart failure, congenital or valvular heart disease, cardiomyopathy, arhythmia, advanced kidney (creatinine > 1.3 mg/dL) or liver disease, psychiatric disease, history of pelvic trauma, and pelvic surgery.

Initial Evaluation

History taking included a patient’s personal history, special habits, duration and type of diabetes, associated medical diseases (hypertension, dyslipidemia), diabetic treatment, and ED history. History of chronic diabetic complications, including retinopathy and neuropathy, was obtained. General examination included weight, height, body mass index, and blood pressure.

Laboratory Investigations

Patients’ glycemic control was evaluated by fasting blood glucose level, glycosylated hemoglobin level, and homeostasis model assessment of insulin resistance. Hemoglobin, high-sensitive C-reactive protein, prostate-specific antigen, and uric acid were evaluated because they could reflect cardiovascular risk burden. Diabetic nephropathy was evaluated by measuring albumin, urine β-microglobulins, serum creatinine, and estimated glomerular filtration rate. Patients with albuminuria (albumin > 30 mg/L) were considered to have nephropathy. A complete lipid profile, including triglyceride, very low-density lipoprotein cholesterol, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, ratio of total cholesterol to high-density lipoprotein cholesterol, apolipoprotein A1, and apolipoprotein B, was obtained. Hormonal assessment of total and free testosterone, luteinizing hormone, and follicle-stimulating hormone levels was performed.

Erectile Function Evaluation

Patients’ erectile function was evaluated by three validated tools. The first tool was the Sexual Health Inventory for Men (SHIM) questionnaire, which evaluated erectile function during the past 6 months. According to the SHIM score, patients were categorized as having mild ED (17–21), mild to moderate ED (12–16), moderate ED (8–11), or severe ED (1–7). The second tool was the erection hardness score (EHS). According to the EHS, patients were categorized as having optimal erection (grade = 4), suboptimal erection (grade = 3), moderate ED (grade = 2), or severe ED (grade = 1). The third tool was the maximal penile circumferential change (MPCC) using an erectometer (Nippon Medical Products, Asahikawa, Japan) during sleep for three nights. The MPCC measurement has a good correlation with the RigiScan and EHS. The ED cutoff point was an MPCC less than 20 mm, as reported in previous studies.

Evaluation of SMI

A 64-row MDCT scanner (Sensation Cardiac 64; Somatom, Munich, Germany) was used to evaluate patients. Before MDCT
Table 1. Patients’ clinical and laboratory characteristics (N = 20)*

| Parameter                                           | Mean ± SD, median (25th–75th percentile), or percentage | Range          |
|-----------------------------------------------------|--------------------------------------------------------|----------------|
| **History**                                         |                                                        |                |
| Age (y)                                              | 61.45 ± 10.7                                          | 42–81          |
| Smoking                                             | 55                                                     |                |
| Smoking history (y)                                 | 37 (14–47)                                            | 7–61           |
| Cigarettes/d                                        | 20 (12.86–33.33)                                      | 1–100          |
| Brinkman smoking index                              | 848.18 ± 453.91                                       | 48–1480        |
| Diabetes duration (y)                               | 6 (4–15)                                               | 1–20           |
| ED history (y)                                      | 3 (2–7)                                                | 1–25           |
| Hypertension                                        | 45                                                     |                |
| Dyslipidemia                                        | 30                                                     |                |
| Retinopathy                                         | 0                                                      |                |
| Neuropathy                                          | 5                                                      |                |
| Diabetes treatment: oral hypoglycemic/insulin        | 55/45                                                  |                |
| **General examination**                             |                                                        |                |
| Weight (kg)                                         | 74.09 ± 17.04                                         | 32.6–114       |
| Height (cm)                                         | 167.46 ± 5.82                                         | 159–179.7      |
| BMI (kg/m²)                                         | 26.33 ± 5.94                                          | 12.9–41.87     |
| Systolic blood pressure (mmHg)                      | 134 ± 14.17                                           | 120–164        |
| Diastolic blood pressure (mmHg)                     | 74.6 ± 7.89                                           | 60–88          |
| **Laboratory investigations**                       |                                                        |                |
| Fasting blood glucose (mg/dL)                       | 139.5 (121.5–189)                                     | 80–413         |
| HbA1c (%)                                           | 7.38 ± 1.21                                           | 5.8–10.6       |
| HOMA-IR (μU/mL)                                     | 15.55 (6.95–37.75)                                    | 1–104.8        |
| hsCRP (mg/dL)                                       | 0.092 (0.021–0.461)                                   | 0.02–1.285     |
| Hb (g/dL)                                           | 14.95 ± 1.32                                          | 12.8–17.7      |
| PSA (ng/mL)                                         | 1.03 (0.47–1.63)                                      | 0.2–13.91      |
| Uric acid (mg/dL)                                   | 5.94 ± 1.17                                           | 3.7–7.3        |
| Albuminuria (mg/L)                                  | 20.65 (9.8–51.95)                                     | 6.5–1403       |
| Diabetic nephropathy                                | 35                                                     |                |
| Urine β₂-microglobulins (μg/L)                      | 38 (29–113)                                           | 15–322         |
| Creatinine (mg/dL)                                  | 0.77 ± 0.2                                            | 0.44–1.11      |
| Estimated glomerular filtration rate (mL/min/1.73 m²)| 89.26 ± 26.9                                         | 49.5–140       |
| Triglyceride (mg/dL)                                | 157.98 ± 91.05                                        | 46–424         |
| VLDL cholesterol (mg/dL)                            | 31.58 ± 18.21                                         | 9.2–71.6       |
| Total cholesterol (mg/dL)                           | 178 ± 36.88                                           | 117–271        |
| HDL cholesterol (mg/dL)                             | 44.24 ± 9.35                                          | 27–59          |
| Total cholesterol/HDL ratio                         | 3.7 (3.4–4.9)                                         | 2.98–6.69      |
| LDL cholesterol (mg/dL)                             | 104.06 ± 23.68                                        | 60–144         |
| Apolipoprotein A₁ (mg/dL)                           | 143.8 ± 23.23                                         | 111–191        |
| Apolipoprotein B (mg/dL)                            | 92.47 ± 11.96                                         | 65–110         |
| Total testosterone (ng/mL)                          | 5.53 ± 2                                              | 2.99–10        |
| Free testosterone (pg/mL)                           | 7.75 ± 2.46                                           | 4–13.8         |
| LH (mIU/mL)                                         | 6.1 (5.1–7.7)                                         | 1.8–27.34      |
| FSH (mIU/mL)                                        | 8.66 (7.4–11.45)                                      | 3.3–50.03      |
| **Erectile function evaluation**                    |                                                        |                |
| SHIM score                                          | 5 (2.5–8.5)                                           | 1–16           |
| EHS                                                 | 2 (1–2)                                                | 1–3            |
| MPCC (mm)                                           | 14.5 ± 9.46                                           | 2.33–32        |

BMI = body mass index; ED = erectile dysfunction; EHS = erection hardness score; FSH = follicle-stimulating hormone; Hb = hemoglobin; HbA1c = glycosylated hemoglobin; HDL = high-density lipoprotein; HOMA-IR = homeostasis model assessment of insulin resistance; hsCRP = high sensitive C-reactive protein; LDL = low-density lipoprotein; LH = luteinizing hormone; MPCC = maximal penile circumferential change; PSA = prostate-specific antigen; SHIM = Sexual Health Inventory for Men; VLDL = very low-density lipoprotein.

*Variables with a normal distribution are expressed as mean ± SD. Variables not normally distributed are expressed as median (25th–75th percentile). Categorical variables are expressed as percentage. The Shapiro-Wilk test was used for testing the normality of the variables.
Data are expressed as number of patients (percentage).

Obstructive CAD (luminal diameter as having obstructive CAD (\(\leq 50\%\)) angiography (N = 70) severe (70\% to 99\%) or non-obstructive CAD (<50\%).35 The number of stenotic vessels (one, two, or three) was estimated. Also, coronary artery stenosis was classified according to coronary artery nomenclature (right, left main trunk, left anterior descending, and left circumflex coronary arteries). Patients with positive MDCT-CA results were informed and followed up (follow-up data incomplete).

**Statistical Analysis**

Correlations between age and maximum stenosis by MDCT-CA and between EHS and maximum stenosis by MDCT-CA were performed using the Pearson correlation test with a two-tailed P value. To identify predictors of SMI, multivariate regression analysis using age and EHS was performed. JMP 11.0 (SAS Institute, Cary, NC, USA) was used for data analysis. A P value less than .05 was considered significant.

**MAIN OUTCOME MEASURES**

The main outcome measurements were the SHIM score, the EHS, MPCC, and coronary artery stenosis by MDCT-CA.

**RESULTS**

The study included 20 patients with diabetes and ED (mean age = 61.45 ± 10.7 years). Most patients had type 2 diabetes (95\%) for a median of 6 years (range = 1–20 years). Associated comorbidities were smoking (55\%), hypertension (45\%), and dyslipidemia (30\%). All data related to the patients’ characteristics, including history, general examination, laboratory investigations, and erectile function, are presented in Table 1. Erectile function evaluation according to the SHIM score was 5 (range = 1–16); 75\% had severe ED (score ≤ 7) and 25\% had mild to moderate (score = 12–16) or moderate (score = 8–11) ED. The patients’ EHS was 2 (range = 1–3), and 78.9\% of patients had an EHS no higher than 2. The MPCC was 11.66 (range = 2.33–32), and 64.3\% of patients had an MPCC less than 20 mm.

MDCT-CA showed positive coronary artery stenosis in 65\% of subjects. Fifty percent of patients showed obstructive CAD (\(\geq 50\%\) lumen obstruction). One-vessel CAD (30\%) was the commonest presentation. The left anterior descending coronary artery was the commonest coronary artery with stenosis. Data related to MDCT-CA are presented in Table 2. Fifteen percent (3 of 20) of patients had greater than 90\% stenosis, and two of them underwent an immediate coronary angioplasty with stenting to prevent myocardial infarction. Maximum coronary

| Parameter | Grades | n (%) |
|-----------|--------|-------|
| MDCT-CA result | Positive coronary artery stenosis | 13 (65) |
| MDCT-CA according to CAD obstruction | Non-obstructive CAD (<50%) | 3 (15) |
| | Obstructive CAD (\(\geq 50\%\)) | 10 (50) |
| Quantitative MDCT-CA stenosis grading | Minimal (<25%) | 1 (5) |
| | Mild (25–49%) | 2 (10) |
| | Moderate (50–69%) | 3 (15) |
| | Severe (70–99%) | 7 (35) |
| | Severe (>90%) | 3 (15) |
| MDCT-CA according to number of affected vessels | 1-vessel CAD | 6 (30) |
| | 2-vessel CAD | 2 (10) |
| | 3-vessel CAD | 5 (25) |
| MDCT-CA according to affected vessels | RCA | 7 (35) |
| | LMT | 2 (10) |
| | LAD | 11 (55) |
| | LCX | 6 (30) |

CAD = coronary artery disease; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; LMT = left main trunk coronary artery; MDCT-CA = multidetector computed tomographic coronary angiography; RCA = right coronary artery.

*Data are expressed as number of patients (percentage).
artery stenosis was positively correlated with age ($P = .016$, $r = 0.529$; Figure 1) and negatively correlated with EHS ($P = .046$, $r = -0.449$; Figure 2). Multivariate regression analysis using age and EHS showed that age was the only independent predictor for SMI ($P = .04$; Table 3). A representative MDCT-CA result of one patient is shown in Figure 3.

**DISCUSSION**

The present study examined the magnitude of the effect of ED on cardiovascular status in diabetic patients using the non-invasive diagnostic modality of MDCT-CA. The present study is the first to use MDCT-CA in patients with asymptomatic diabetes and ED; other studies have used MDCT-CA to investigate patients with only diabetes or patients with only ED. For the relation between ED and CAD, Montorsi et al proposed the artery size hypothesis, which states that when the penile arteries are smaller (1–2 mm) than the coronary arteries (3–4 mm), the penile vasculature is affected sooner by cardiovascular risk factors, which makes ED a predictor of CVD events. The association between ED and CVD events is well established, especially in diabetic patients. Therefore, ED should be considered an independent CVD risk until proved otherwise.

In the present study, MDCT-CA depicted coronary artery stenosis in 65% of patients with ED and asymptomatic CAD. The rate of CAD in diabetic patients with concomitant ED is controversial. One study of patients with asymptomatic diabetes screened with MDCT-CA showed stenosis in 36.5% (19 of 52). The present study found that SMI was very common in diabetic patients with ED without any cardiac symptoms and signs. It showed that 50% of patients had significant obstructive CAD (≥50% decrease in vessel lumen) and 25% of patients had three-vessel CAD. This is considered an alarming sign because obstructive CAD and three-vessel CAD were reported as predictors of all cardiac events after more than 5 years of follow-up of 405 diabetic patients. In addition, left anterior descending coronary artery stenosis was reported in 55% of patients, which was associated with worst prognosis among other myocardial infarction types owing to a larger infarct, especially with advanced age. Therefore, ED identification, especially in diabetic patients younger than 60 years, could assist in CVD risk evaluation and decrease the risk of an event.

A significant positive correlation was observed between ED severity and maximum coronary artery stenosis by MDCT-CA in diabetic patients. The present results are supported by studies that used MDCT-CA to screen patients with ED. In diabetic patients, increasing ED severity was associated with increased total CVD risk, with poor CVD prognosis. Therefore, ED could be used as a warning sign for SMI. The leading interval from ED to CVD events was estimated at 2 to 5 years. In diabetic patients, ED is a predictor of CAD and cardiac events, with a 1.4-fold higher CAD risk compared with diabetic patients without ED. Therefore, ED in diabetic patients is considered an atherosclerosis marker that could assist in the detection of subclinical vascular disorders. In patients with diabetes and ED, SMI has been screened using different stress tests, showing that the presence vs absence of ED can improve the sensitivity of screening guidelines for SMI in diabetic patients.

In the present study, age was the only predictor for coronary artery stenosis in diabetic patients with ED. This result is consistent with that of a study that showed that increasing age was an independent risk factor for a high Agatston coronary artery calcium score in patients with ED. In another study, ED predicted CAD in patients with type 2 diabetes without clinically evident CVD. A prospective study found that predictors of SMI were diabetes duration, intima-media thickness, and statin therapy at MDCT-CA screening of patients with asymptomatic diabetes. Recently, MDCT-CA screening of 320 patients with asymptomatic diabetes showed that glycosylated hemoglobin level of at least 7.4%, dyslipidemia, diabetes duration, and retinopathy were predictors for SMI. Therefore, MDCT might be helpful to identify CAD in diabetic patients with ED and high risk for CVD (including aging) in the future. Radiation exposure from these screening modalities also should be considered.

The present study has several limitations. The sample was extracted from outpatients who presented at our clinic seeking for treatment for ED. Thus, the subjects were from a strongly biased population. Furthermore, we could not set the controls; therefore,

**Table 3. Multivariate regression analysis to identify predictors of silent myocardial ischemia using age and EHS parameters**

| Variable | Sum of square | F ratio | $P$ value |
|----------|---------------|---------|-----------|
| Age      | 4,439,132     | 4,932   | .0402     |
| EHS      | 2,483,168     | 2,759   | .150      |

EHS = erection hardness score.
we could not compare the CAD prevalence in diabetic patients with ED with other combinations of disease status, such as subjects with vs without diabetes and/or with vs without ED. Comparative data on CAD prevalence in diabetic patients are needed. In addition, CAD should be assessed separately for type 1 and for type 2 diabetes owing to different pathogeneses and outcomes. The sample size was limited; therefore, only two parameters (age and ED severity) were used to assess the predictive factor for SMI. We did this to distinguish the stronger predictor for CAD, and we believe this information is important for patients with diabetes and ED. The diagnosis of CAD in diabetic patients with ED was performed using only MDCT-CA, which is an indicator of atherosclerosis but cannot assess inducible ischemia as stress testing can. Also, coronary artery calcium scoring was not calculated for the MDCT-CA scan because we used coronary artery stenosis grading as an outcome measurement for the MDCT-CA results. In the future, a large-scale comparative study including healthy men should be performed.

**CONCLUSIONS**

CAD was highly prevalent (65%) in diabetic patients with ED in our outpatient clinic. Furthermore, 15% of patients showed severe coronary artery stenosis (≥90%), which might lead to myocardial infarction. Age was the single significant predictor for coronary artery stenosis in diabetic patients with ED. One should consider the possibility of SMI in elderly patients with diabetes who have ED.

**Corresponding Author:** Shigeo Horie, Department of Urology, Juntendo University, Hongo 2-1-1, Tokyo, Bunkyo-ku 113-8421, Japan. Tel: 81-3-3813-3111; Fax: 81-3-5802-1227; E-mail: shorie@juntendo.ac.jp

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**STATEMENT OF AUTHORSHIP**

**Category 1**

(a) **Conception and Design**

Amr Abdelhamed; Shin-ichi Hisasue; Essam A. Nada; Ali A. Kassem; Mohammed Abdel-Kareem; Shigeo Horie

(b) **Acquisition of Data**

Amr Abdelhamed; Shin-ichi Hisasue; Shigeo Horie

Figure 3. Representative multidetector computed tomographic coronary angiographic result showing stenosis of the RCA, LAD, and CX in an 81-year-old man with diabetes and erectile dysfunction. CX = left circumflex coronary artery; LAD = left anterior descending coronary artery; RCA = right coronary artery.
REFERENCES

1. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010;87:4-16.

2. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention; 2011. p. 1-12.

3. Roger VL, Go AS, Lloyd-Jones DM, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. Circulation 2012;125:e2-220.

4. Fowler MJ. Microvascular and macrovascular complications of diabetes. Clin Diabetes 2008;26:77-82.

5. Gandaglia G, Briganti A, Jackson G, et al. A systematic review of the association between erectile dysfunction and cardiovascular disease. Eur Urol 2014;65:968-978.

6. Malavige LS, Levy JC. Erectile dysfunction in diabetes mellitus. J Sex Med 2009;6:1232-1247.

7. Yamada T, Hara K, Umematsu H, et al. Erectile dysfunction and cardiovascular events in diabetic men: a meta-analysis of observational studies. PLoS One 2012;7:e43673.

8. Corona G, Rastrelli G, Silverii A, et al. The identification of prediabetes condition with ARIC algorithm predicts long-term CV events in patients with erectile dysfunction. J Sex Med 2013;10:1114-1123.

9. Corona G, Fagiolli G, Mannucci E, et al. Penile Doppler ultrasound in patients with erectile dysfunction (ED): role of peak systolic velocity measured in the flaccid state in predicting arteriogenic ED and silent coronary artery disease. J Sex Med 2008;5:2623-2634.

10. Tabibiazar R, Edelman SV. Silent ischemia in people with diabetes: a condition that must be heard. Clin Diabetes 2003;21:5-9.

11. Valensi P, Lorgis L, Cottin Y. Prevalence, incidence, predictive factors and prognosis of silent myocardial infarction: a review of the literature. Arch Cardiovasc Dis 2011;104:178-188.

12. Fox CS, Golden SH, Anderson C, et al; American Heart Association Diabetes Committee of the Council on Lifestyle and Cardiometabolic Health, Council on Clinical Cardiology, Council on Cardiovascular and Stroke Nursing, Council on Cardiovascular Surgery and Anesthesia, Council on Quality and Outcomes Research, American Diabetes Association. Update on prevention of cardiovascular disease in adults with type 2 diabetes mellitus in light of recent evidence: a scientific statement from the American Heart Association and the American Diabetes Association. Diabetes Care 2015;38:1777-1803.

13. Davis TM, Coleman RL, Holman RR. Prognostic significance of silent myocardial infarction in newly diagnosed type 2 diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS) 79. Circulation 2013;127:980-987.

14. Scheidt-Nave C, Barrett-Conner E, Wingard DL. Resting electrocardiographic abnormalities suggestive of asymptomatic ischemic heart disease associated with non-insulin-dependent diabetes mellitus in a defined population. Circulation 1990;81:899-906.

15. Doobay AV, Anand SS. Sensitivity and specificity of the ankle-brachial index to predict future cardiovascular outcomes: a systematic review. Arterioscler Thromb Vasc Biol 2005;25:1463-1469.

16. Prevalence of unrecognized silent myocardial ischemia and its association with atherosclerotic risk factors in noninsulin-dependent diabetes mellitus. Milan Study on Atherosclerosis and Diabetes (MiSAD) Group. Am J Cardiol 1997;79:134-139.

17. Young LH, Wackers FJ, Chyun DA, et al; DIAD Investigators. Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. JAMA 2009;301:1547-1555.

18. Lièvre MM, Moulin P, Thivolet C, et al; DYNAMIT investigators. Detection of silent myocardial ischemia in asymptomatic patients with diabetes: results of a randomized trial and meta-analysis assessing the effectiveness of systematic screening. Trials 2011;12:23.

19. Elkeles RS, Godsland IF, Feher MD, et al; PREDICT Study Group. Coronary calcium measurement improves prediction of cardiovascular events in asymptomatic patients with type 2 diabetes: the PREDICT study. Eur Heart J 2008;29:2244-2251.

20. Scholte AJ, Schuijf JD, Kharagjitsingh AV, et al. Prevalence of silent coronary artery disease: combined use of stress myocardial perfusion imaging and coronary calcium scoring. JACC Cardiovasc Imaging 2009;2:131-138.

21. Scholte AJ, Bax JJ, Wackers FJ. Screening of asymptomatic patients with type 2 diabetes mellitus for silent coronary artery disease: combined use of stress myocardial perfusion imaging and coronary calcium scoring. J Nucl Cardiol 2006;13:11-18.

22. Khan A, Khosa F, Nasir K, et al. Comparison of radiation dose and image quality: 320-MDCT versus 64-MDCT coronary angiography. AJR Am J Roentgenol 2011;197:163-168.

23. Meijer AB, OYL, Geleijns J, et al. Meta-analysis of 40- and 64-MDCT angiography for assessing coronary artery stenosis. AJR Am J Roentgenol 2008;191:1667-1675.

24. Nishioka H, Furukawa N, Shimoda S, et al. Predictors of coronary heart disease in Japanese patients with type 2 diabetes:...
screening for coronary artery stenosis using multidetector computed tomography. J Diabetes Invest 2010;1:50-55.

25. Andreini D, Pontone G, Mushtaq S, et al. Prognostic value of multidetector computed tomography coronary angiography in diabetes: excellent long-term prognosis in patients with normal coronary arteries. Diabetes Care 2013;36:1834-1841.

26. Yaman O, Gulpinar O, Hasan T, et al. Erectile dysfunction may predict coronary artery disease: relationship between coronary artery calcium scoring and erectile dysfunction severity. Int Urol Nephrol 2008;40:117-123.

27. Jackson G. Erectile dysfunction and asymptomatic coronary artery disease: frequently detected by computed tomography coronary angiography but not by exercise electrocardiography. Int J Clin Pract 2013;67:1159-1162.

28. Umul M, Semerci B, Umul A, et al. Relationship between erectile dysfunction and silent coronary artery disease: detection with multidetector computed tomography coronary angiography. Urol Int 2014;92:310-315.

29. Standards of medical care in diabetes—2013. Diabetes Care 2013;36(Suppl. 1):S11-S66.

30. Cappelleri JC, Rosen RC. The Sexual Health Inventory for Men (SHIM): a 5-year review of research and clinical experience. Int J Impot Res 2005;17:307-319.

31. Mulhall JP, Goldstein I, Bushmakin AG, et al. Validation of the erection hardness score. J Sex Med 2007;4:1626-1634.

32. Suzuki K, Sato Y, Horita H, et al. The correlation between penile tumescence measured by the erectometer and penile rigidity by the RigiScan. Int J Urol 2001;8:594-598.

33. Matsuda Y, Hisasue S, Kumamoto Y, et al. Correlation between erection hardness score and nocturnal penile tumescence measurement. J Sex Med 2014;11:2272-2276.

34. Raff GL, Abidov A, Achenbach S, et al; Society of Cardiovascular Computed Tomography. SCCT guidelines for the interpretation and reporting of coronary computed tomographic angiography. J Cardiovasc Comput Tomogr 2009;3:122-136.

35. Montorsi P, Ravagnani PM, Galli S, et al. The artery size hypothesis: a macrovascular link between erectile dysfunction and coronary artery disease. Am J Cardiol 2005;96:19m-23m.

36. Guo W, Liao C, Zou Y, et al; ADVANCE Collaborative Group. Erectile dysfunction and later cardiovascular disease in men with type 2 diabetes: prospective cohort study based on the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation) trial. J Am Coll Cardiol 2010;56:1908-1913.

37. Batty GD, Li Q, Czernichow S, et al; ADVANCE Collaborative Group. Erectile dysfunction and later cardiovascular disease in men with type 2 diabetes: prospective cohort study based on the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified-Release Controlled Evaluation) trial. J Am Coll Cardiol 2010;56:1908-1913.

38. Montorsi P, Ravagnani PM, Galli S, et al. Association between erectile dysfunction and coronary artery disease: matching the right target with the right test in the right patient. Eur Urol 2006;50:721-731.

39. Kyto V, Sipila J, Rautava P. Association of age and gender with anterior location of STEMI. Int J Cardiol 2014;176:1161-1162.

40. Miner M, Seftel AD, Nehra A, et al. Prognostic utility of erectile dysfunction for cardiovascular disease in younger men and those with diabetes. Am Heart J 2012;164:21-28.

41. Meena BL, Kohar DK, Agarwal TD, et al. Association between erectile dysfunction and cardiovascular risk in individuals with type-2 diabetes without overt cardiovascular disease. Int J Diabetes Dev Ctries 2009;29:150-154.

42. Heruti RJ, Uri I, Arbel Y, et al. Erectile dysfunction severity might be associated with poor cardiovascular prognosis in diabetic men. J Sex Med 2007;4:465-471.

43. Jackson G, Boon N, Eardley I, et al. Erectile dysfunction and coronary artery disease prediction: evidence-based guidance and consensus. Int J Clin Pract 2010;64:848-857.

44. Gandaglia G, Salonia A, Passoni N, et al. Erectile dysfunction as a cardiovascular risk factor in patients with diabetes. Endocrinology 2013;43:285-292.

45. González-Juanatey JR, Alegria Ezquerra E, Gomis Barberá R, et al; Estudio DIVA. [Erectile dysfunction as a marker of silent cardiovascular disease in type-2 diabetic patients in Spain. The DIVA (Diabetes and VAscular disease) study]. Med Clin 2009;132:291-297 [in Spanish].

46. Gazzaruso C, Giordanetti S, De Amici E, et al. Relationship between erectile dysfunction and silent myocardial ischemia in apparently uncomplicated type 2 diabetic patients. Circulation 2004;110:22-26.

47. Gazzaruso C, Solerte SB, Pujia A, et al. Erectile dysfunction as a predictor of cardiovascular events and death in diabetic patients with angiographically proven asymptomatic coronary artery disease: a potential protective role for statins and 5-phosphodiesterase inhibitors. J Am Coll Cardiol 2008;51:2040-2044.

48. García-Malpartida K, Mármol R, Jover A, et al. Relationship between erectile dysfunction and silent myocardial ischemia in type 2 diabetic patients with no known macrovascular complications. J Sex Med 2011;8:2606-2616.

49. Gazzaruso C, Coppola A, Montalcini T, et al. Erectile dysfunction can improve the effectiveness of the current guidelines for the screening for asymptomatic coronary artery disease in diabetes. Endocrinology 2011;40:273-279.

50. Ma RC, So WY, Yang X, et al. Erectile dysfunction predicts coronary heart disease in type 2 diabetes. J Am Coll Cardiol 2008;51:2045-2050.

51. Shimabukuro M, Saito T, Higa T, et al. Risk stratification of coronary artery disease in asymptomatic diabetic subjects using multidetector computed tomography. Circ J 2015;79:2422-2429.