

## ERECTILE DYSFUNCTION

# Relation Between Erectile Dysfunction and Silent Myocardial Ischemia in Diabetic Patients: A Multidetector Computed Tomographic Coronary Angiographic Study



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## 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 =  $61.45 \pm 10.7$  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.

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

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## 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.<sup>1</sup> Most patients with diabetes (90–95%) have type 2 diabetes mellitus.<sup>2</sup> The death rate of diabetic adults is two to four times higher than for non-diabetic adults,<sup>2</sup> with cardiovascular disease (CVD) being the commonest cause of death.<sup>3</sup> 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).<sup>4</sup> 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.<sup>5</sup>

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.<sup>6</sup> A meta-analysis has associated ED with increased risk of CVD events in diabetic patients.<sup>7</sup> Even prediabetes identification in patients with ED has been associated with CVD predication.<sup>8</sup> Penile color Doppler ultrasound has been recognized as a potential tool for predicting silent myocardial ischemia (SMI) in patients with ED.<sup>9</sup>

Patients with SMI exhibit objective findings suggestive of myocardial infarction in the absence of angina or equivalent symptoms.<sup>10</sup> 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.<sup>11</sup> Several studies have been conducted to screen for SMI in patients with diabetes using different tools with varying sensitivity and specificity,<sup>12</sup> including electrocardiography,<sup>13,14</sup> the ankle-brachial index,<sup>15</sup> nuclear myocardial perfusion imaging studies,<sup>16–18</sup> coronary artery calcium scoring using electron-beam computed tomography or multidetector computed tomography (MDCT),<sup>19,20</sup> or a combination of such tests.<sup>21</sup>

MDCT coronary angiography (MDCT-CA) has become a reliable non-invasive imaging modality with high specificity and sensitivity for the evaluation of CAD.<sup>22,23</sup> MDCT-CA has been used to screen patients with asymptomatic diabetes for SMI,<sup>24</sup> providing long-term prognostic value.<sup>25</sup> Some studies have used MDCT-CA to screen for SMI in patients with ED.<sup>26–28</sup> 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.<sup>29</sup> Exclusion criteria included patients with cerebrovascular disease, congestive heart failure, congenital or valvular heart disease, cardiomyopathy, arrhythmia, 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  $\beta$ -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 A<sub>1</sub>, 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).<sup>30</sup> 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).<sup>31</sup> 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<sup>32</sup> and EHS.<sup>33</sup> The ED cutoff point was an MPCC less than 20 mm, as reported in previous studies.<sup>32</sup>

## Evaluation of SMI

A 64-row MDCT scanner (Sensation Cardiac 64; Somatom, Munich, Germany) was used to evaluate patients. Before MDCT

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