Rationale and design for

the Liaoning Diabetic Microvascular Complications Study (LD-MCS)

Registry Objectives

Liaoning Diabetic Microvascular Complications Study (LD-MCS) is a serial epidemiological study of microangiopathy in type 2 diabetes from hospital registry in Liaoning Province, China. It includes three sub-studies: diabetic retinopathy (DR), diabetic peripheral neuropathy (DPN) and diabetic nephropathy (DN). All participants involved in LD-MCS were recruited at the First Affiliated Hospital of China Medical University (CMU1h). The CMU1h is located in Shenyang City, situated in the northern-east part of China, and functions as a National key discipline for both Endocrine and Metabolic disease. DR sub-study of LD-MCS is aimed to investigate the potential risk factors and effective clinical biomarkers of retinopathy by statistical analysis methods, further clarifying the mechanism of its generation and progression. It is anticipated to develop an early warning system of DR based on multivariable-adjusted models, so as to achieve timely detection and better prognosis for patients with type 2 diabetes.

Ethics

This study was approved by the Institutional Review Board (IRB) of the CMU1h (AF-SOP-07-1.1-01/2019-13).

Registry Population

LD-MCS established a retrospective hospital-based cohort database, which continuously records the data of all hospitalized patients from February 2012 to November 2018. All of them were Chinese adults (≥ 18 years old) registered as the confirmed type 2 diabetes in Department of Diabetic Eye Disease Center, or Endocrinology and Metabolism of the CMU1h. Type 2 diabetes was defined as fasting plasma glucose (FPG) ≥ 7.0 mmol/l (no caloric intake over 8 h), two-hour plasma glucose ≥ 11.1 mmol/l in an oral glucose tolerance test (OGTT), hemoglobin A1c (HbA1c) ≥ 6.5% (48 mmol/mol), random plasma glucose ≥ 11.1 mmol/L with classic symptoms of hyperglycemia or hyperglycemia crisis, self-reported previous clinician-diagnosed diabetes or use of anti-diabetic agents, according to the criteria of the American Diabetes Association Standards of diabetes care. Patients who died or had a history of non type 2 diabetes were exculed. Consenquently, this hospital-registry database of LD-MCS totally enrolled 5,066 available subjects for analysis.

Exposure

Two-field fundus photographs which centered on the optic disk and fovea was performed by trained photographers, using non-mydriatic fundus camera (CR6-45NM; Canon, Inc., Japan) in a double-blind condition. The presence of DR was diagnosed from the worse eye at the Department of Ophthalmology of the

CMU1h. Abiding by the criterion of Early Treatment for Diabetic Retinopathy Study (ETDRS), the diagnosis of DR was confirmed as the following fundus lesions: microaneurysms, haemorrhagia, cotton-wool spots, retinal microvascular damage, hard exudation, venous beading and neovascularization. DR was rated as 4 severity scales, included mild non-proliferative DR (NPDR), moderate NPDR, severe NPDR and proliferative DR (PDR). Clinically significant macular edema (CSME) was defined by the presence of retinal hard exudates within the central fovea area. Severe NPDR, PDR and/or CSME was defined as vision-threaten DR (VTDR). Among the entire participants with type 2 diabetes, 1,469 (29.0%) of them were diagnosed as DR, the proportion of mild NPDR, moderate NPDR and VTDR was 18.7% (n = 946), 4.3% (n = 217), and 6.0% (n = 306) respectively.

5. Design of Variables

Each participant was requested to complete a comprehensive assessment at the time of his/her initial admission, covering personal information, medical history, physical examination, clinical feature, laboratory results, and disease diagnosis. The detailed records were captured in a centrally managed online hospital information system, and its items were shown in Table 1.

Table 1

Included variables in hospital-registry database of LD-MCS.

Item	Included variables
General information	Registry number, gender, age, date of birth, duration of diabetes, status of smoking and alcohol-drinking, family history of diabetes and hypertension, use of anti-diabetic agents, and etc.
Anthropometric parameters	Height, weight, BMI, HR, SBP, DBP, and PP.
Clinical data	HbA1c, OGTT, Ins, CPS, IAA, GADA, lipid profile, liver function test, myocardial zymogram test, renal function test, blood coagulation function test, autoimmune disease antibody, tumor marker, bone metabolism marker, thyroid function test, serum ion, blood routine examination, urine analysis, sex hormone test, and etc.
DR	The occurrence and severity of DR.

Abbreviations: BMI, body mass index; CPS, c-peptide release test; DBP, diastolic blood pressure; GADA, anti-glutamic acid decarboxylase antibody; HbA1c, hemoglobin A1c; HR, heart rate; IAA, insulin autoantibody; Ins, insulin release test; OGTT, oral glucose tolerance test; PP, pulse pressure; SBP, systolic blood pressure.

Explanation:

i. General information was completed by filling a personal details questionnaire without other interference.

ii. Anthropometric parameters were measured by medical professionals. Height (cm) was measured by a wall-mounted stadiometer and a portable horizontal headboard on a firm ground as the base, while weight (kg) was measured by a calibrated electronic digital scale on the flat floor. BMI (kg/m^2) was calculated as weight divided by the square of height. Blood pressure (mmHg) and HR (bmp) were measured by calibrated electronic sphygmomanometers under a quiet status or after at least 10-minute sitting. PP was calculated as SBP minus DBP.

iii. Clinical data stemmed from the test of blood and urines samples at the Department of Clinical Laboratory of the CMU1h, which were collected in the morning from individuals after an overnight fasting (at least 8 hours without calorie intaking).