SUPPLEMENTAL METHODS

This prospective study included 690 individuals with type 2 diabetes from the Rio de Janeiro Type 2 Diabetes Cohort Study, enrolled between August 2004 and December 2008 and re-evaluated annually until December 2019 in the diabetes outpatient clinic of our tertiary care University Hospital. The study was approved by the Research Ethics Committee of the School of Medicine and University Hospital, Federal University of Rio de Janeiro, Brazil (number124/2004), and all participants gave written informed consent. Exclusion criteria to enter the cohort were a body mass index >40 kg/m^2, serum creatinine ≥180 mmol/L and the presence of any serious concomitant disease, such as hepatic, pulmonary or cancer. All patients gave written informed consent and local Ethics Committee previously approved the study. All patients were submitted to a standard protocol that included a complete clinical examination, with particular attention to the presence of micro and macrovascular degenerative complications, five clinical tests of cardiovascular autonomic function, laboratory evaluation, resting 12-lead electrocardiogram, 24-hour ambulatory blood pressure monitoring and a 2-D echocardiogram. Only patients in sinus rhythm on electrocardiogram entered this study [18-21].

Office blood pressure was measured three times using a digital oscillometric blood pressure monitor (HEM-907 XL, Omron Healthcare, Kyoto, Japan) with a suitable sized cuff. The first measure was discarded and blood pressure considered was the mean between the two last readings. Pulse pressure was calculated as systolic blood pressure (SBP) minus diastolic blood pressure (DBP). Arterial hypertension was diagnosed if mean SBP ≥140 or DBP ≥90 mm Hg or if anti-hypertensive drugs had been prescribed.

Coronary heart disease was diagnosed by clinical, or electrocardiographic criteria (Minnesota codes: 1.1–1.3, 4.1–4.4, or 5.1–5.3), or by positive ischemic stress tests. Cerebrovascular disease was diagnosed by history and physical examination and peripheral arterial disease by systolic ankle-braquial index <0.9. Diabetic retinopathy was evaluated by an ophthalmologist. The diagnosis of nephropathy needed at least two urinary albumin excretion rate ≥30 mg/day or proteinuria ≥0.5 g/day or confirmed reduction of glomerular filtration rate (creatinine clearance <1 mL/sec or serum creatinine >130 μmol/L). Peripheral neuropathy was ascertained by clinical examination (knee and ankle reflex activities, feet sensation with the Semmes-Weinstein 5.07 [10 g] monofilament and vibration, using a 128-Hz tuning fork).