RESEARCH

Telemedicine assists in the management of proatherogenic dyslipidemia and postprandial glucose variability in patients with type 2 diabetes mellitus: a cross-sectional study

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Abstract

Objective: Coronary heart disease (CHD) is a prevalent complication of type 2 diabetes mellitus (T2DM). The proatherogenic low-density lipoprotein (LDL) cholesterol is an established risk factor of cardiovascular disease, and evidence also suggests that postprandial plasma glucose (PPG) levels closely delineate CHD mortality in diabetes. The investigators hypothesized that the addition of telehealth consultation to standard antidiabetic therapy may help to reduce postprandial glucose variability and plasma LDL cholesterol levels in patients with T2DM.

Methods: This cross-sectional study enrolled patients with newly diagnosed T2DM who received standard antidiabetic therapy with or without additional telehealth consultation. Participants received blood tests for plasma lipid profile and glucose levels at the diagnosis of diabetes and after 1 month of therapeutic intervention. Laboratory results were compared between treatment groups to determine the efficacy of complementary telehealth consultation.

Results: In this study, 375 participants were enrolled. The standard treatment group had considerably greater levels of plasma LDL cholesterol than recipients of telehealth consultation (110 mg/dL vs 93.1 mg/dL, $P < 0.001$). Moreover, patients receiving standard treatment had greater levels of fasting plasma glucose (104 mg/dL vs 98.5 mg/dL, $P = 0.027$), 2-h PPG (169 mg/dL vs 111 mg/dL, $P < 0.001$), and postprandial glucose variability (65.4 mg/dL vs 12.8 mg/dL, $P < 0.001$) than participants under telehealth consultation.

Conclusions: Telemedicine in addition to standard antidiabetic therapy helped to reduce plasma LDL cholesterol levels and postprandial glucose variability in patients with newly diagnosed T2DM. Therefore, telehealth consultation is a suitable complement to pharmacologic therapy for diabetic patients to assist in the management of proatherogenic dyslipidemia and postprandial glucose variability.

Key Words

- type 2 diabetes mellitus
- telehealth
- hyperlipidemia
- glucose variability

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Introduction

Type 2 diabetes mellitus (T2DM) is a metabolic disease that induces substantial morbidity in affected patients (1). Chronic hyperglycemia predisposes patients to microvascular complications including retinopathy, neuropathy, and kidney dysfunction (2). Importantly, diabetes is also linked to macrovascular diseases such

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as coronary heart disease (CHD) and peripheral arterial disease (3). Indeed, cardiovascular disease is a prevalent risk factor of mortality in T2DM (4), and prevention of diabetic CHD is an essential component of diabetes management guidelines (5, 6).

Diabetic dyslipidemia has several unique features. Insulin resistance increases the flux of free fatty acids to the liver, which leads to excessive plasma triglycerides (TG), reduced high-density lipoprotein (HDL) cholesterol, and oxidized low-density lipoprotein (LDL) cholesterol (7). Among these lipoprotein fractions, LDL cholesterol contributes to atheroma formation in blood vessels and is an established risk factor of CHD (8). Therefore, plasma LDL cholesterol is a suitable target for the prevention of diabetic cardiovascular disease (9).

Recently, postprandial glucose variability has garnered attention as a potential risk factor for cardiovascular complications. In the Whitehall study, the cardiovascular risk increased in line with postprandial glucose levels (10). Moreover, a European research consortium observed that 2-h postprandial plasma glucose (PPG) levels correlated with cardiovascular risk in T2DM (11). Therefore, investigators have proposed that postprandial hyperglycemia may be a risk factor of diabetic CHD (12).

Telemedicine is a complementary therapeutic modality in the treatment of T2DM. Conventional antidiabetic therapy based on drug prescriptions may lead to inadequate glycemic control (13). Importantly, individuals with newly diagnosed T2DM confront challenges including dietary choices and sick day management (14). Without adequate support from medical professionals, patients can experience diabetes-related distress that interferes with diabetes self-care (15). In contrast, telehealth consultation can provide timely and accurate information that leads to better compliance and clinical outcome (16).

Currently the effect of telemedicine on diabetic dyslipidemia and postprandial glucose variability remains uncertain. In this study, the investigators hypothesized that the addition of telehealth consultation to standard antidiabetic therapy may help to improve plasma lipid profile and postprandial glucose variability in patients with newly diagnosed T2DM.

Materials and methods

Study population

This cross-sectional study was conducted at a medical center in Taiwan. Candidates visiting the Endocrinology clinic between October 2014 and September 2016 were screened for eligibility. Inclusion criteria were as follows: (i) patients over 21 years of age, (ii) newly diagnosed T2DM according to the diagnostic criteria of the American Diabetes Association, namely, serum glycosylated hemoglobin A1c (HbA1c) level ≥ 6.5%, fasting plasma glucose (FPG) ≥ 126 mg/dL, 2-h PPG after 75-g oral glucose tolerance test ≥ 200 mg/dL, or random plasma glucose levels ≥ 200 mg/dL with classic symptoms of diabetes, (iii) no concomitant prescription of antidiabetic or lipid-lowering medications, and (iv) compliance with blood tests and dietary instructions.

Exclusion criteria were as follows: (i) patients with familial hypercholesterolemia, chronic kidney disease, hypothyroidism, or hemoglobin disorders, (ii) chronic alcoholism, or (iii) recipients of estrogen replacement or antidepressants.

Study protocol

Demographic data including age, sex, body weight, and height were recorded at the initial clinic visit. Thereafter, two treatment groups were established according to shared decision-making between patients and their attending physicians. The control group received metformin prescription and medical nutrition consultation at disease diagnosis and during monthly clinic appointments. The telemedicine group received telehealth consultation during workdays in addition to metformin prescription. Participants maintained their therapeutic regimens for 1 month prior to follow-up laboratory tests.

Medical nutrition consultation

Participants received one session of medical nutrition consultation at disease diagnosis and during monthly clinic appointments. Certified diabetes educators provided 30 min of comprehensive consultation according to current guidelines (5). Specifically, patients were instructed to limit saturated fat to less than 5% of total calories and increase whole grain intake. Furthermore, participants learned the carbohydrate counting technique and their daily recommended carbohydrate intake.

Telehealth consultation

For the group receiving telemedicine, each participant was assigned to a diabetes educator who provides consultation via telephone or messaging software during workdays. The messaging software was provided by the Health2Sync

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developer that allows participants to upload photographs of daily meals and plasma glucose readings from finger-stick glucose meters. Diabetes educators assess data collected by Health2Sync and contact their corresponding participants once a week to monitor dietary habits and medication use.

Laboratory evaluation

Participants received blood tests for serum creatinine, serum alanine transaminase, HbA_{1c}, and plasma lipid profile after a 12-h fast at the initial clinic visit. These patients consumed a meal consisting of 75 g of carbohydrates, 5 g of fat, and 10 g of protein, and PPG levels were measured 2 h afterward. Participants could modify the content of their meals, for instance, forgoing fruit juice or snacks, according to their dietary choices.

Patients maintained their therapeutic regimens and returned for follow-up after 1 month. At the follow-up appointment, participants fasted for 12 h before venous sampling for plasma TG, LDL cholesterol, HDL cholesterol, and FPG. Subsequently, patients consumed a meal with the previously mentioned nutritional composition. Once again, participants were given an option to alter the content of the meal, and venous sampling for PPG level was performed 2 h afterward.

Blood samples were delivered to the central laboratory within 1 h of venous sampling and assayed by Beckman Coulter UniCel DxC 800 Synchron Clinical Systems. The analytical precision was within 1.7 mg/dL for HDL cholesterol, within 3.0 mg/dL for LDL cholesterol, within 7.5 mg/dL for TG, and within 2.0 mg/dL for plasma glucose level. The plasma LDL cholesterol level was measured by the timed endpoint method using a commercial polyanion solution.

Ethics approval

This study was conducted in accordance to the World Medical Association's Declaration of Helsinki. The protocol was approved by the Institutional Review Board of Changhua Christian Hospital (CCH IRB No. Y_107_0195). Participants provided written informed consent to take part in the study.

Statistical analysis

Study outcomes including age, gender, mean serum HbA_{1c}, plasma glucose levels, and lipid profile were compared between therapeutic groups using independent *t*-test for continuous variables and Pearson's χ^2-test for categorical variables. Statistical analysis was performed using Statistical Package for the Social Sciences (version 22.0, SPSS, Chicago, IL), with a two-sided *P* value of less than 0.05 interpreted as statistically significant.

Results

This study screened 385 patients visiting the endocrinology clinic for eligibility. Six individuals were excluded due to chronic kidney disease, and four patients were ineligible due to coexisting hypothyroidism. The enrollment protocol is illustrated in Fig. 1.

Demographic characteristics of the participants at diagnosis

The study enrolled 375 participants who were divided into two therapeutic groups according to shared decision making with their attending physicians. As demonstrated in Table 1, demographic characteristics of the participants including age, sex, serum HbA_{1c}, BMI, blood pressure, serum creatinine, and serum alanine transaminase were similar between treatment groups. Patients in each group also had similar plasma metabolic profile and received comparable dose of metformin therapy.

Effect of telemedicine and standard treatment on plasma lipid profile after 1 month

As observed in the study, participants in both groups had similar levels of plasma TG (177 mg/dL vs 179 mg/dL, $P=0.824$) and HDL cholesterol (56.1 mg/dL vs 53.9 mg/dL, $P=0.133$). However, patients in the standard treatment group had considerably greater levels of plasma LDL cholesterol than recipients of additional telemedicine (110 mg/dL vs 93.1 mg/dL, $P < 0.001$). These findings are summarized in Table 2.

Effect of telemedicine and standard treatment on plasma glucose levels after 1 month of treatment

As shown in Table 3, recipients of standard treatment had greater levels of FPG than those receiving additional telehealth consultation (104 mg/dL vs 98.5 mg/dL, $P=0.027$). Furthermore, participants receiving standard treatment had higher 2-h PPG relative to those under telemedicine (169 mg/dL vs 111 mg/dL, $P < 0.001$). Postprandial plasma glucose variability, defined as the difference between 2-h PPG and FPG levels, was also higher

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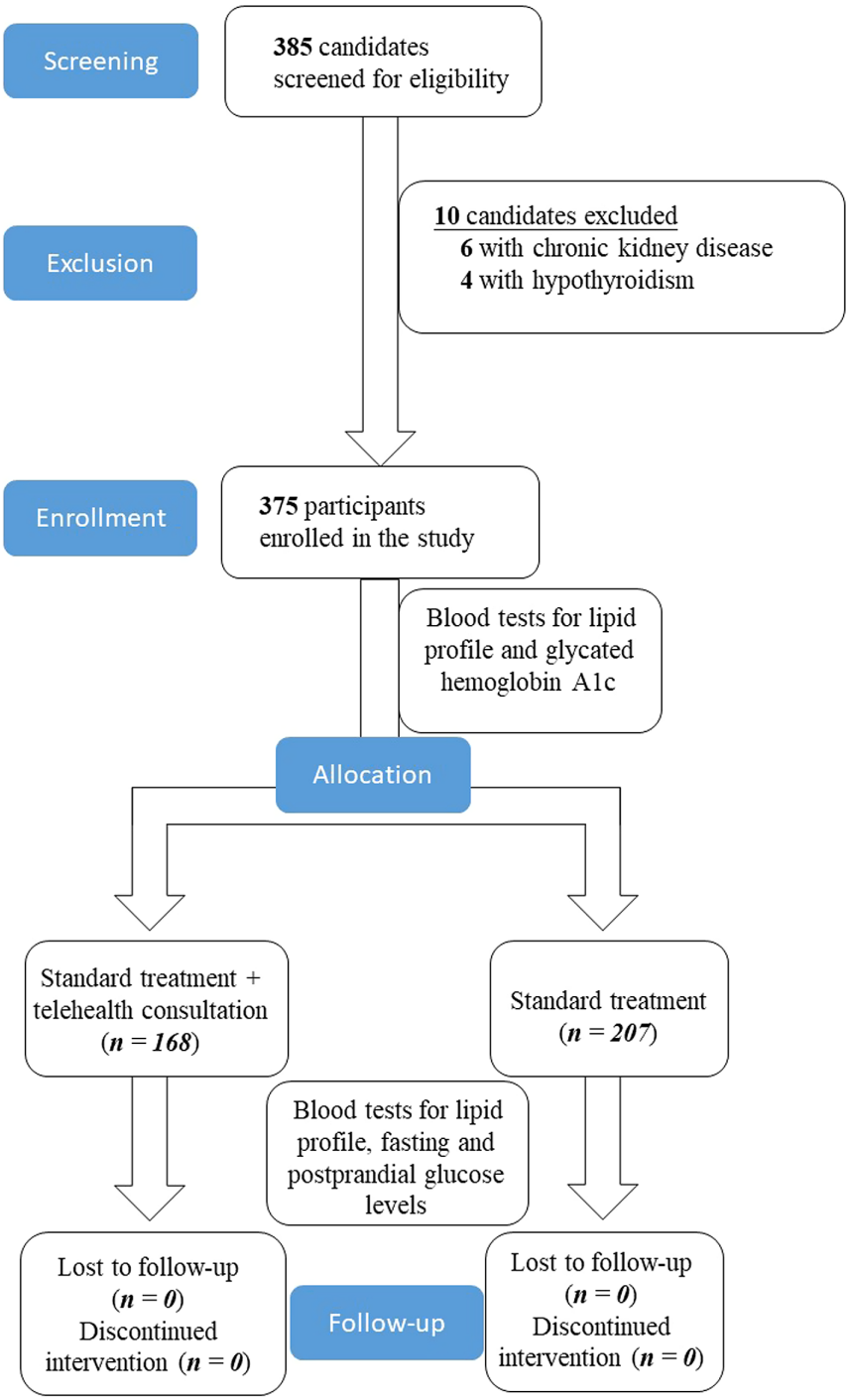

Figure 1
Enrollment protocol of the study.

in standard treatment compared to the telemedicine group (65.4 mg/dL vs 12.8 mg/dL, $P < 0.001$).

Discussion

This study observed that recipients of standard antidiabetic therapy had greater plasma LDL cholesterol levels than patients under telemedicine. Moreover, patients receiving standard therapy harbored higher levels of FPG, 2-h PPG, and postprandial glucose variability compared to recipients of a telehealth consultation.

Telemedicine may help to improve diabetic dyslipidemia and glucose variability by providing accurate information about dietary choices (17). Indeed, clinic appointments rarely provide diabetic patients with

Table 1 Demographic features of the participants at diagnosis of diabetes.

Parameters	Standard treatment + telemedicine ($n = 168$)	Standard treatment ($n = 207$)	*P* value
Age (years)	66.9 ± 12.0	64.9 ± 13.1	0.116
Sex (Female)	92 (54.8%)	108 (52.2%)	0.617
Serum HbA_{1c} (%)	9.1 ± 2.2	9.3 ± 2.3	0.334
Fasting plasma glucose level (mg/dL)	169 ± 6.3	170 ± 6.1	0.132
2-h postprandial plasma glucose level (mg/dL)	243 ± 34.6	239 ± 35.5	0.446
Body weight (kg)	54.9 ± 10.7	54.6 ± 11.2	0.766
Body height (m)	1.45 ± 0.07	1.46 ± 0.20	0.795
Body mass index (kg/m^2)	25.9 ± 4.2	25.8 ± 4.8	0.837
Systolic blood pressure (mm Hg)	157 ± 19.5	158 ± 19.4	0.786
Diastolic blood pressure (mm Hg)	63.0 ± 9.2	63.2 ± 8.1	0.817
Serum creatinine (mg/dL)	0.67 ± 0.19	0.68 ± 0.19	0.583
Serum alanine transaminase (U/L)	42.5 ± 29.5	41.6 ± 29.8	0.788
Plasma triglycerides (mg/dL)	230 ± 124	216 ± 108	0.267
Plasma high-density lipoprotein cholesterol (mg/dL)	57.8 ± 23.3	58.5 ± 16.3	0.744
Plasma low-density lipoprotein cholesterol (mg/dL)	124 ± 47.4	127 ± 46.3	0.575
Metformin dose (mg per day)	1313 ± 470	1345 ± 488	0.508

Data are expressed as means with standard deviation of the mean for continuous variables and number (percentage) for categorical variables. Variables are compared between groups using independent *t*-test for continuous variables and Pearson's χ^2-test for categorical variables.
A1c, mm Hg, millimeters of mercury; HbA_{1c}, glycosylated haemoglobin; kg, kilograms; m, meters; mg, milligrams.

adequate self-care skills due to inexperienced medical staff (18). Moreover, common misconceptions about T2DM warrant discussion with diabetes educators (19). For example, herbal medicine may adversely influence glycemic control, which can be promptly discussed with the patients during telemedicine sessions (20).

Furthermore, contact with healthcare professionals can improve adherence to a healthy lifestyle and antidiabetic medications (21, 22). This study has shown that telemedicine can promote appropriate dietary choices, leading to lower postprandial glucose variability. Indeed, a preceding study has shown that nutrition consultation at clinic visits rarely provides sufficient self-care skills to diabetic patients (23).

Postprandial glucose variability can exacerbate diabetic CHD through several mechanisms. Transient hyperglycemia induces proinflammatory micro-RNA particles that disrupt the endothelial function of coronary arteries (24). Furthermore, glucose variability is positively correlated with an arterial intimal thickness (25), a measure of intravascular atheroma burden. This study demonstrated that telemedicine can help to lower postprandial glucose variability and maybe a complementary therapeutic option for diabetic CHD.

Since LDL cholesterol is an established risk factor of diabetic CHD (26), even modest lowering of this lipoprotein by telemedicine may help to attenuate cardiovascular mortality. Moreover, this study observed that telemedicine has a complementary role in alleviating plasma glucose variability. Considering that hyperglycemia is central to diabetic microvascular complications (27), telemedicine in addition to pharmacologic intervention may lead to better diabetes care.

The strength of this study includes a sizeable population enrolled from the endocrinology clinic, which renders the findings applicable to general practice. Diabetes educators provided medical nutrition therapy to participants to ensure similar levels of dietary lipid intake. Participants received metformin prescription, which can reduce the confounding effect of different antidiabetic medications on plasma glucose levels.

Nonetheless, this study has several limitations. First, 2-h PPG was assessed by consuming a standard meal and

Table 2 Effect of telemedicine and standard treatment on plasma lipid profile.

Parameters	Standard treatment + telemedicine ($n = 168$)	Standard treatment ($n = 207$)	*P* value
Plasma triglycerides (mg/dL)	179 ± 97.7	177 ± 88.7	0.824
Plasma high-density lipoprotein cholesterol (mg/dL)	53.9 ± 14.5	56.1 ± 13.9	0.133
Plasma low-density lipoprotein cholesterol (mg/dL)	93.1 ± 29.0	110 ± 27.1	<0.001

Data are expressed as means with standard deviation of the mean for continuous variables. Variables are compared between groups using independent *t*-test.
mg/dL, milligrams per decilitre.

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Table 3 Effect of telemedicine and standard treatment on plasma glucose levels.

Parameters	Standard treatment + telemedicine (n = 168)	Standard treatment (n = 207)	*P* value
Fasting plasma glucose level (mg/dL)	98.5 ± 21.1	104 ± 26.1	0.027
2-h postprandial plasma glucose level (mg/dL)	111 ± 22.8	169 ± 44.7	<0.001
Glucose variability (mg/dL)	12.8 ± 7.3	65.4 ± 35.1	<0.001

Glucose variability is defined as the difference between 2-h postprandial and fasting plasma glucose levels.
kg, kilograms; m, meters; mg, milligrams; mg/dL, milligrams per decilitre; mm Hg, millimeters of mercury.

may not reflect a patient's daily dietary habits. Moreover, additional factors that influence postprandial glucose levels, such as the metabolic syndrome or insulin resistance, were unaccounted for in the study. Finally, the insulin secretory reserve of the pancreas can modify postprandial glucose levels but was not quantified in the study.

In conclusion, recipients of standard antidiabetic therapy had greater plasma LDL cholesterol levels and postprandial glucose variability than participants under telemedicine. Therefore, telemedicine may be a complementary option to assist in the management of proatherogenic dyslipidemia and glucose variability in diabetes.

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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