Diabetes, Metabolic Syndrome and Obesity

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ORIGINAL RESEARCH

The Importance of Clinical Pharmacists in Improving Blood Glucose and Lipid Levels in Patients with Diabetes and Myocardial Infarction

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Purpose: The aim of this study was to evaluate whether intervention by clinical pharmacists can improve blood glucose and lipid levels in diabetic patients with complex medical conditions.

Methods: The retrospective database included 138 patients with diabetes who had presented with acute myocardial infarction (AMI) between January 2019 and October 2021. Blood glucose and lipid levels were measured within 12 weeks and 78 weeks of follow-up. Propensity score matching (PSM) was used to balance the confounding effects of patients' characteristics.

Results: A total of 138 eligible patients were assigned to either the intervention group (n = 47) or the usual care group (n = 91). After the intervention, there were significant improvements in blood glucose (glycosylated hemoglobin-HbA1C % from 9.0 to 8.3; fasting blood glucose-FBG mmol/L from 11.3 to 7.1; postprandial blood glucose-PBG mmol/L from 17.0 to 12.1; $p < 0.001$) and lipid levels (total cholesterol-TC from 4.9 to 3.5, low-density lipoprotein cholesterol-LDL-C from 3.0 to 1.8, $p < 0.001$, mmol/L) in both follow-up periods. The blood glucose effects were most pronounced in the PBG control rate (76.9% vs 54.0%) before PSM, while HbA1C% and PBG control rate after PSM were significantly higher in the intervention group (HbA1C% rate: 65.6% vs 38.5%; PBG rate: 79.2% vs 45.8%; $p < 0.05$, intervention vs non-intervention). Subgroup analysis further confirmed the improvement of blood glucose and lipid mainly in patients with higher baseline FBG (≧10mmol/L) and moderate follow-up duration (4–12 weeks).

Conclusion: The intervention of clinical pharmacists in multidisciplinary team can significantly improve blood glucose and lipid levels in complex type 2 diabetic patients, especially those with high baseline FBG and moderate follow-up durations.

Keywords: blood glucose, blood lipid, clinical pharmacist's intervention, propensity score matching, complex diabetes

Introduction

The global diabetes prevalence in 20–79 adults was estimated to be 10.5% in 2021 and will rise to 12.2% in 2045, from 536.6 to 783.2 million people. Diabetes mellitus (DM) has become one of the most serious and common chronic diseases in the worldwide, which will cause life threatening, disabling and acute or chronic complications, consequently reduce life expectancy.[1] DM is a common comorbidity among patients with acute myocardial infarction (AMI), affecting almost 30% of cases.[2] DM is a major and independent risk factor, increasing mortality by nearly two-fold during both the acute and long-term follow-up period, compared to those without diabetes.[3] Hospitalized patients with AMI who have high blood glucose levels after admission are at a significantly increased risk of mortality and adverse outcomes. Studies have reported an 18% increase in the risk of cardiovascular disease (CVD) for every one percentage point increase in

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glycosylated hemoglobin (HbA1C).[4] Complex diabetes refers to patients with major or multiple comorbidities, requiring high-touch multidisciplinary care and sustainable support for self-management.[5] Individuals with both diabetes and CVD have a high incidence of poor glycemic control and are one of the main forms of complex diabetes.

Hyperglycemia is known to directly and indirectly worsen myocardial damage in AMI, including by exacerbating left ventricular remodeling through increased interstitial fibrosis and myocyte apoptosis, as well as microvascular dysfunction by promoting platelet-dependent thrombosis and elevating circulating adhesion molecules.[6] Hyperglycemia typically arises from defects in insulin secretion and action. As an important anabolic hormone, insulin deficiency and resistance can lead to abnormalities in lipid metabolism, while abnormal lipid levels can in turn worsen the progression of diabetes.[7,8] Thus, dyslipidemia is a negative prognostic factor for AMI patients. Various epidemiological studies and randomized clinical trials (RCTs) have identified that certain lipid profiles, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), are closely connected with cardiovascular safety.[9–11] In particular, LDL-C concentration is directly linked to major cardiovascular events (MACE), with a 1.0 mmol/L reduction associated with a weighted average reduction of 22% in first MACE and mainly a 29% reduction in non-fatal myocardial infarction.[12] As such, effective management of blood glucose and lipid levels in complex diabetes is both important and urgent.

Clinical pharmacists currently play a vital role in the multidisciplinary glucose management team by providing pharmaceutical care to enhance the rational use of medications for patients with diabetes. Compared to standard care, pharmacist interventions have led to favorable improvements in blood glucose indexes such as HbA1C, blood glucose, and cardiovascular risk factors, as well as blood pressure, lipid levels, and body weight.[13,14] As a result, we have established a new blood glucose management model that is coordinated by clinical pharmacists and clinicians. Previous studies have confirmed the effectiveness of pharmacist involvement in blood glucose management in hospitals, particularly in improving blood glucose fluctuations in patients with comorbid diabetes and AMI.[15,16] However, these studies did not examine the long-term efficacy of this management model on blood glucose and lipid levels in follow-up. Therefore, the aim of this study is to evaluate the long-term effects of the coordinated management model by clinical pharmacists and clinicians on blood glucose and lipid levels in patients with comorbid diabetes and AMI.

Materials and Methods

Study Population

The study population comprised patients with a history of DM who were admitted to our institution for AMI between January 2019 and October 2021 and had follow-up data available. The eligibility criteria for the study were as follows: (1) a diagnosis of diabetes, (2) a diagnosis of AMI, including both ST-segment elevation myocardial infarction (STEMI) and non-ST elevation myocardial infarction (NSTEMI), (3) treatment with oral or intravenous anti-hypoglycemic drugs, (4) availability of follow-up data from the electronic record, and (5) age 18 years or older. Patients were excluded if their blood glucose or lipid data were unavailable or if the first follow-up interval exceeded one and a half years. The study was approved by the ethics committees of Ren Ji Hospital, Shanghai Jiao Tong University School of Medicine (KY2019-076), and informed consent was obtained from each patient or their guardians.

The Role of Pharmacists on the Multidisciplinary Team

We utilized a previously established multidisciplinary pharmacist-clinician team model to manage blood glucose, lipid, and other related variables in patients with AMI and diabetes.[15,16] Clinical pharmacists are responsible for inpatient pharmaceutical consultations and post-discharge pharmaceutical follow-ups. Those with specialized training in endocrinology have extensive expertise in managing the glucose levels of diabetic patients, honed over five years of experience. For inpatient pharmaceutical consultations, pharmacists offer consultations through a combination of face-to-face and telemedicine appointments. Clinicians can request consultations using an electronic system and await confirmation. Before each consultation, the pharmacist assesses the patient's condition, analyzes their medications, and identifies any potential drug-related issues, creating a tailored treatment plan. Additionally, pharmacists will visit the patient to provide instructions on diet, exercise, and medication. While face-to-face interviews are used for complex cases, noncomplicated

cases can be managed through the Renji App, a mobile electronic case system that also enables the monitoring of blood glucose levels.

Specifically speaking, Renji App is an official hospital App in the institution, we can get through patient's information, exam and test reports, blood glucose data at any time. For noncomplicated patients, we conducted a comprehensive analysis of patient information and gave physicians an electronic consultation sheet. Furthermore, changes in the blood glucose and lipid regimen and communication between physicians and pharmacists are always via Wechat or telephone. Comparable procedures are followed in other hospitals, albeit with slight variations in the request and confirmation process. After discharge, clinical pharmacists invite patients to participate in a joint medical follow-up three months later at the outpatient clinic to confirm medication adherence, check for adverse drug reactions, and identify any issues with medication use. Any medication-related problems that arise are promptly resolved, and patients are encouraged to follow their doctor's orders. Additionally, a telephone follow-up is conducted monthly to track any medication-related issues the patient may have.

Specific Pharmacist Interventions for Blood Glucose and Lipid Control

The specific pharmacist interventions aimed to improve blood glucose and lipid control mainly consisted of two parts: consultation-based health education and drug optimization. Firstly, for each patient, an individualized target was set based on their unique characteristics such as BMI, liver and renal functions, duration of diabetes, and other comorbidities. Secondly, a customized health education plan was developed by specialized pharmacists, including dietary guidelines, such as food type, dining order, dining way, and total quantity, as well as individualized exercise guidelines, such as time, frequency, intensity, and types of sports. Lastly, the pharmacist optimized the patient's medication regimen based on their specific glucose and lipid goals.

Data Collection

We collected patients' demographic information, diabetes-related variables, and lipid-related variables by reviewing the hospital electronic record system. Blood glucose-related data included venous fasting blood glucose (FBG), 2-hour postprandial blood glucose (PBG), and glycosylated hemoglobin (HbA1C). Lipid profile data included the concentrations of total, low-density lipoprotein (LDL), small-dense low-density lipoprotein (sd-LDL), high-density lipoprotein (HDL), non-high-density lipoprotein (non-HDL) cholesterol, as well as triglycerides (TG). Follow-up data from the medical charts and hospital information systems were obtained to explore the long-term effects of pharmacist interventions. The first follow-up was considered to be less than or equal to 12 weeks, and the second follow-up was considered to be between 12 and 78 weeks.

Outcomes Measures

The study's outcomes focused on blood glucose and lipid variables. The blood glucose data mainly included FBG, PBG, and HbA_{1C}, and the blood lipid data mainly contained TC, TG, LDL-C, HDL-C, non-HDL-C, and sd-LDL-C. The standard glucose target was considered as target 1 and met the following criteria according to Chinese guidelines:[17,18] HbA_{1C} less than 8.0%, FBG between 7.8 and 10.0 mmol/L, PBG between 7.8 and 13.9 mmol/L. Meanwhile, the blood lipid standard target was regarded as target 2, which mainly referred to three composite indicators of TC, TG and LDL-C. The lipid level met the following criteria under the Chinese guidelines:[19,20] TC less than 4.5 mmol/L, TG less than 1.7 mmol/L, LDL-C less than 1.4 mmol/L.

Data Analyses

Continuous variables were reported as mean with standard error (SE), and categorical variables were reported as counts and percentages. The comparison between the pharmacist intervention and non-intervention groups was analyzed using independent sample Student's *t*-tests or Wilcoxon signed-rank tests for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Paired Student's *t*-tests were used to compare data before and after follow-up in the intervention group. To adjust for differences in baseline characteristics between intervention and non-intervention groups, we used propensity score matching (PSM).[21] Propensity scores were generated using logistic regression modeling of the patients' probability based on the baseline characteristics listed in Table 1. The matching tolerance used for matching was assessed by calculating absolute

Table 1 Characteristics of Patients with Diabetes and Acute Myocardial Infarction in Intervention or Non-Intervention Before and After Propensity Score Matching

Characteristics	Before PSM		After PSM	
	No Intervention (n=91)	Intervention (n=47)	No Intervention (n=42)	Intervention (n=42)
Patients baseline				
Age (year)	63.6±1.0	63.7±1.9	63.9±1.5	62.2±1.9
Body weight (kg)	71.7±1.2	67.3±2.2	70.3±11.9	68.0±2.3
BMI (kg/m^2)	25.6±0.3	24.9±0.6	25.4±0.4	25.0±0.6
Diabetic data				
Diabetic duration (year)	8.8±0.9	10.6±1.4	9.7±1.5	11.6±1.5
HbA1c %	8.6±0.2	9.0±0.2	8.8±0.2	8.7±0.2
FBG (mmol/L)	9.7±0.3	11.3±0.4**	10.8±0.5	10.9±0.5
PBG (mmol/L)	16.3±0.5	17.0±0.7	16.9±0.8	16.3±0.6
Lipid data				
TC (mmol/L)	4.9±0.1	4.9±0.2	4.9±0.2	4.9±0.2
TG (mmol/L)	2.0±0.1	1.9±0.2	1.8±0.2	2.0±0.2
HDL-C (mmol/L)	1.0±0.0	1.1±0.0*	1.1±0.0	1.1±0.0
LDL-C (mmol/L)	3.0±0.1	3.0±0.2	3.1±0.2	3.0±0.2
non-HDL-C (mmol/L)	3.9±0.1	3.8±0.2	3.9±0.2	3.8±0.2
sd-LDL-C (mmol/L)	1.0±0.0	0.8±0.1*	1.0±0.1	0.8±0.1

Notes: Data were described as mean±SE, *p<0.05, **p <0.01.

Abbreviations: BMI, body mass index. Diabetic duration was counted in years. Diabetic and lipid data were collected from venous blood. FBG, fasting blood glucose; PBG, postprandial blood glucose; HbA1c%, glycosylated hemoglobin; TC, total cholesterol; TG, triacylglycerol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; non-HDL-C, non-high density lipoprotein cholesterol; sd-LDL-C, small-dense low density lipoprotein cholesterol.

standardized differences in covariates between groups, and a recommended balance value of 0.02 was used in this study. Subgroup analysis was also conducted by different baseline FBG (FBG ≦10 mmol/L and FBG >10 mmol/L) and follow-up durations (≦4 weeks, between 4 and 12 weeks, between 12 and 24 weeks, 24 and 78 weeks). A P value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS 26.0 software (SPSS Inc.).

Results

Patients' Characteristics

Figure 1 illustrates the flow diagram outlining the process of patient selection. A total of 309 hospitalized cases with diabetes and AMI from electronic health records were initially reviewed, of which 72 patients who received pharmacist consultations were considered as the intervention group, while 237 patients who did not receive pharmacist interventions were considered as the control group. Of these, 171 patients were excluded for reasons such as unavailable efficacy data and unmatched follow-ups, with 25 patients in the intervention group and 146 patients in the non-intervention group. Finally, a total of 138 patients with diabetes were included in the study, with 47 patients in the intervention group and 91 patients in the non-intervention group, meeting the inclusion criteria. The baseline characteristics of patients before and after PSM are presented in Table 1. The mean age, BMI, and diabetic duration of the included patients were 63.6 years, 25.4 kg/m^2, and 9.5 years, respectively. Before PSM, age, body weight, and most indexes of blood glucose and lipid were comparable between the two groups. However, certain blood glucose data were higher in the intervention group, with FBG being the main significant difference. Regarding lipid data, although HDL-C and sd-LDL-C data were significantly different, the absolute values were only slightly different. After PSM, the above indicators were well balanced, resulting in 42 patients in each group.

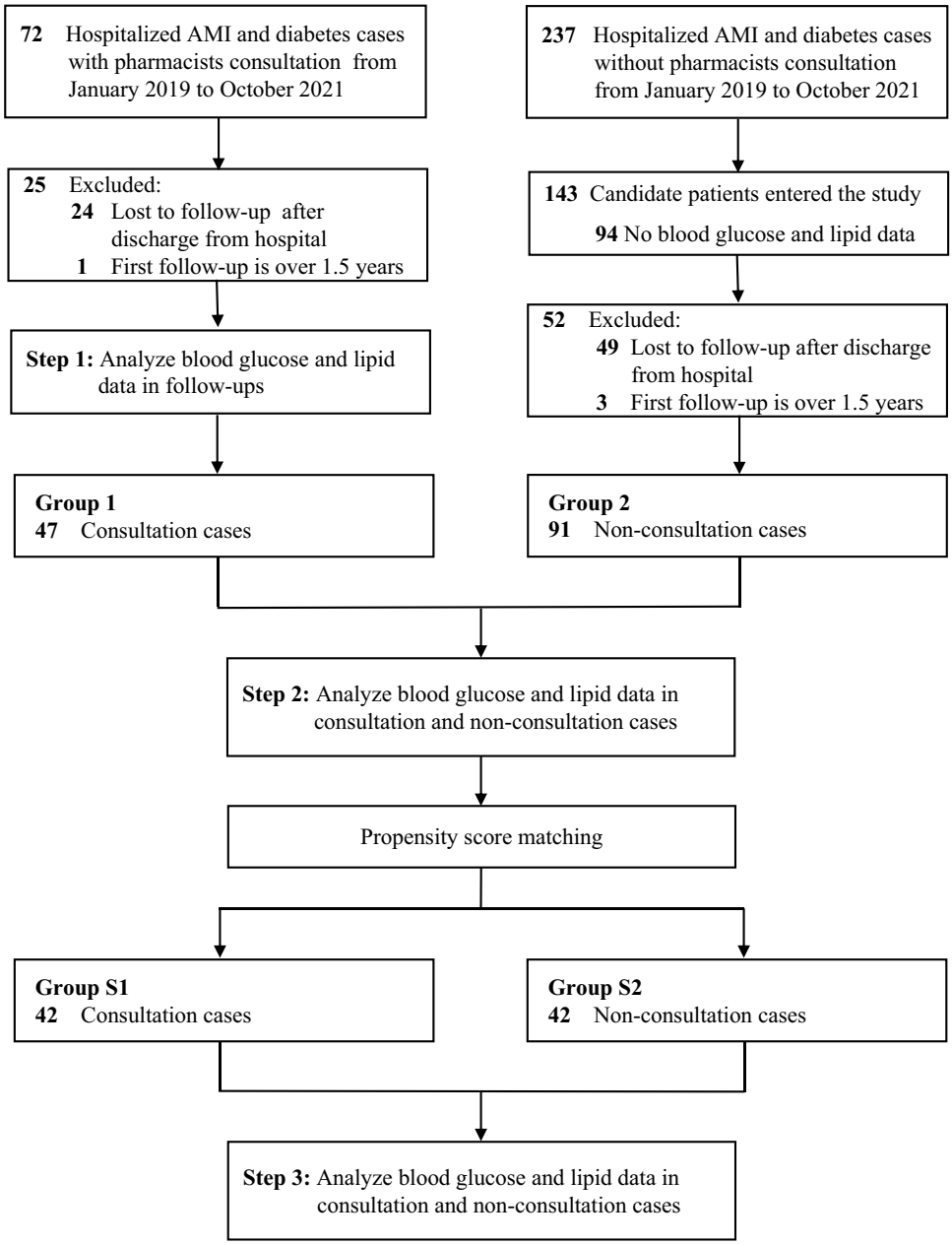

Figure 1 The flow diagram of the selection process to determine eligible individuals.
Abbreviation: AMI, acute myocardial infarction.

Glucose and Lipid Levels in the Intervention Patients

The follow-up periods for the intervention were 42.1 and 203.6 days in the first and second follow-ups, respectively. Table 2 and Table 3 provide details of the follow-up durations and outcomes. As shown in Figure 2, the intervention of the new glucose management model resulted in significant improvements in glycemic control and lipid levels after the first follow-up visit. Specifically, mean HbA1C % decreased from 9.0 to 8.3, mean FBG mmol/L from 11.3 to 7.1, and mean PBG mmol/L from 17.0 to 12.1 ($p < 0.001$). Lipid levels also improved, with mean TC decreasing from 4.9 to 3.5, mean LDL-C from 3.0 to 1.8, mean sd-LDL-C from 0.8 to 0.5, and mean non-HDL-C from 3.8 to 2.6 ($p < 0.001$, mmol/L). However, there was no significant improvement in TG (1.9 mmol/L to 1.8 mmol/L, $p = 0.493$) or HDL-C (1.1 mmol/L to 0.9 mmol/L, $p = 0.001$). In the second follow-up visit, most of the outcomes were consistent with the first follow-up visit, except for PBG, which did not show a significant improvement (mean PBG mmol/L from 17.0 to 13.1, $p = 0.332$).

Table 2 Blood Glucose and Lipid Data in Intervention or Non-Intervention During the First Follow-Up Visit Before and After Propensity Score Matching

First Follow-Up	Before PSM		After PSM	
	No Intervention (n=91)	Intervention (n=47)	No Intervention (n=42)	Intervention (n=42)
Follow up duration (day)	38.0±2.6(68)	42.1±2.8(44)	43.1±4.2(33)	41.5±2.9(40)
Diabetic data				
HbA1c %	8.5±0.2(54)	8.3±0.2(36)	9.0±0.2(26)	8.2±0.2(32)*
FBG (mmol/L)	8.1±0.3(67)	7.1±0.4(43)*	8.5±0.6(32)	7.2±0.4(39)
PBG (mmol/L)	13.3±0.6(50)	12.1±0.6(27)	14.0±1.0(24)	12.1±0.6(25)
Lipid data				
TC (mmol/L)	3.7±0.1(65)	3.5±0.2(41)	3.7±0.2(31)	3.5±0.2(37)
TG (mmol/L)	1.8±0.1(65)	1.8±0.2(41)	1.7±0.1(31)	1.8±0.2(37)
HDL-C (mmol/L)	0.9±0.0(65)	0.9±0.0(41)	1.0±0.0(31)	0.9±0.0(37)
LDL-C (mmol/L)	2.0±0.1(65)	1.8±0.1(41)	2.1±0.2(31)	1.8±0.1(37)
Non-HDL-C (mmol/L)	2.7±0.1(65)	2.6±0.1(41)	2.8±0.2(31)	2.6±0.2(37)
sd-LDL-C (mmol/L)	0.7±0.1(55)	0.5±0.1(36)	0.7±0.1(27)	0.5±0.1(32)

Notes: Follow up duration was counted in days. Diabetic and lipid data were collected from venous blood. Data were described as mean±SE, *p<0.05.
Abbreviations: FBG, fasting blood glucose; PBG, postprandial blood glucose; HbA1c%, glycosylated hemoglobin; TC, total cholesterol; TG, triacylglycerol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; non-HDL-C, non-high density lipoprotein cholesterol; sd-LDL-C, small-dense low density lipoprotein cholesterol.

Table 3 Blood Glucose and Lipid Data in Intervention or Non-Intervention During the Second Follow-Up Visit Before and After PSM

Second Follow-Up	Before PSM		After PSM	
	No Intervention (n=91)	Intervention (n=47)	No Intervention (n=42)	Intervention (n=42)
Follow up duration (day)	219.6±16.0(55)	203.6±22.0(25)	246.9±26.1(26)	199.4±24.5(22)
Diabetic data				
HbA1c %	7.8±0.3(37)	7.9±0.3(21)	7.9±0.4(18)	7.7±0.3(19)
FBG (mmol/L)	7.4±0.4(50)	7.6±0.5(26)	7.7±0.5(24)	7.2±0.4(23)
PBG (mmol/L)	13.6±0.8(20)	13.1±0.9(8)	14.1±0.9(12)	13.1±0.9(8)
Lipid data				
TC (mmol/L)	3.7±0.1(52)	3.6±0.2(26)	3.6±0.2(24)	3.4±0.2(23)
TG (mmol/L)	1.6±0.2(52)	1.5±0.1(26)	1.5±0.2(24)	1.4±0.2(23)
HDL-C (mmol/L)	1.0±0.0(52)	1.0±0.1(26)	1.0±0.0(24)	1.0±0.1(23)
LDL-C (mmol/L)	2.0±0.1(52)	1.9±0.1(26)	1.9±0.1(24)	1.8±0.1(23)
Non-HDL-C (mmol/L)	2.7±0.1(51)	2.5±0.2(26)	2.6±0.2(24)	2.5±0.2(23)
sd-LDL-C (mmol/L)	0.7±0.1(32)	0.6±0.1(14)	0.6±0.1(17)	0.6±0.1(11)

Notes: Follow up duration was counted in days. Diabetic and lipid data were collected from venous blood. Data were described as mean±SE.
Abbreviations: FBG, fasting blood glucose; PBG, postprandial blood glucose; HbA1c%, glycosylated hemoglobin; TC, total cholesterol; TG, triacylglycerol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; non-HDL-C, non-high density lipoprotein cholesterol; sd-LDL-C, small-dense low density lipoprotein cholesterol.

Further analysis revealed that the number of follow-up samples in the second visit was significantly lower than the first visit, which might have contributed to inconsistent results, especially for PBG (27 patients in the first visit versus 8 patients in the second visit). Overall, the pharmacist consultations and new glucose management model demonstrated significant improvements in glycemic control and lipid levels in these complex diabetes patients.

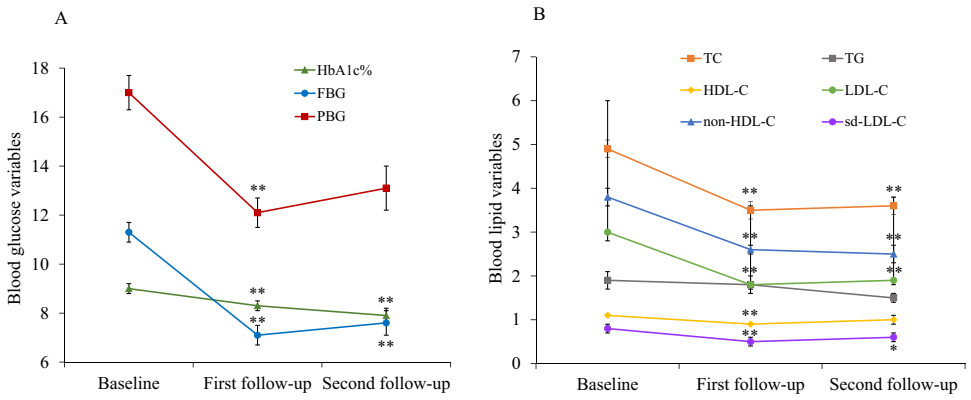

Figure 2 Blood glucose and lipid data from baseline to the follow-ups. Sub-figure (**A**) is for blood glucose data; Sub-figure (**B**) is for lipid data. Blood glucose mainly included glycosylated hemoglobin (HbA_{1C}), fasting blood glucose (FBG), and postprandial blood glucose (PBG). Blood lipid mainly included total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL-C), high- density lipoprotein (HDL-C), and non-high-density lipoprotein (non-HDL-C), and small dense low-density lipoprotein (sd-LDL-C). Data were described as mean±SE (n=47), **p<0.01 and *p<0.05.

Glucose and Lipid Levels in the Intervention and Non-Intervention Patients Before and After PSM

In the first follow-up, prior to PSM, only FBG showed a significant decrease in the intervention group compared to the non-intervention group (7.1 mmol/L vs 8.1 mmol/L, $p < 0.05$). Although other glucose indicators, including HbA1C and PBG, showed no statistical difference, they exhibited a downward trend following the pharmacist's intervention (HbA1C, 8.3% vs 8.5%, $p = 0.413$; PBG, 12.1 mmol/L vs 13.3 mmol/L, $p = 0.199$, intervention versus non-intervention). After PSM, HbA1C was significantly lower in the intervention group compared to the non-intervention group (HbA1C, 8.2% vs 9.0%, $p = 0.015$). However, no clear effects were observed between the two groups in terms of other glucose indexes (FBG and PBG) and lipid levels, except for the lipid composed target 2 (TC, TG, and LDL-C), which showed improvement in lipid management after PSM (Table 2). In the second follow-up, limited sample sizes did not show any significant differences in blood glucose and lipid levels between the two groups, although slight decreases were observed following the pharmacist's intervention (Table 3).

For patients with AMI, glycemic goals should be set at less stringent levels depending on their condition and the reason for admission, such as FBG levels of 7.8–10.0 mmol/L, PBG levels of 7.8–13.9 mmol/L, and HbA1C less than 8.0%.[17,18] Following the pharmacist's intervention, the incidence of blood glucose control was higher in the intervention group than in the non-intervention group after PSM (especially for the targets of HbA1C <8.0%, 65.6% versus 38.5%, and PBG <13.9 mmol/L, 79.2% versus 45.8%). Although no significant effects were observed in FBG and the composed target 1 (HbA1C, FBG, and PBG), upward trends were observed after intervention. The control rate of the lipid composed target 2 (TC, TG, and LDL-C) was 35.1% (13/37) in intervention group compared with 9.7% (3/31) in non-intervention group, indicating an improvement in lipid management after PSM. Notably, the improvement in lipid management was mainly attributed to the control rate of LDL-C (16.1%, 5/31 versus 37.8%, 14/37 in non-intervention compared with intervention group, $p = 0.042$) (Table 4). However, no significant differences were found in lipid profile levels between the intervention and non-intervention groups in the two follow-ups (Table 2 and Table 3).

Subgroup Analysis of Glucose and Lipid Levels in the Intervention and Non-Intervention Patients

The subgroup analysis results for blood glucose and lipid levels are presented in Tables S1–S3. For different baseline FBG levels, compared with non-intervention patients, the pharmacists' intervention was found to exert more favorable effects on HbA1C (non-intervention vs intervention; 9.3 vs 8.6%, $p = 0.049$) and FBG (non-intervention vs intervention; 8.9 vs 8.6 mmol/L, $p = 0.043$) when the FBG restricted to more than 10 mmol/L during the first follow-up duration. Similar download trends have been described for PBG, TC, and LDL-C, but there was no significant different ($p > 0.05$).

Table 4 Blood Glucose and Lipid Stratify According to Standards During the First Follow-Up Visit Before and After PSM

First Follow-Up	Before PSM		After PSM	
	No Intervention	Intervention	No Intervention	Intervention
Diabetic data (%)				
HbA1c%<8.0	57.4(31/54)	61.1(22/36)	38.5(10/26)	65.6(21/32) *
FBG<10 mmol/L	85.1(57/67)	86.0(37/43)	78.1(25/32)	84.6(33/39)
PBG <13.9 mmol/L	54.0(27/50)	76.9(20/26) *	45.8(11/24)	79.2(19/24) *
Target 1	23.9(16/67)	23.3(10/43)	21.9(7/32)	25.6(10/39)
Lipid data (%)				
TC<4.5 mmol/L	80.9(55/68)	82.9(34/41)	77.4(24/31)	83.8(31/37)
TG<1.7 mmol/L	53.0(35/66)	68.3(28/41)	54.8(17/31)	64.9(24/37)
LDL-C<1.4 mmol/L	21.2(14/66)	34.1(14/41)	16.1(5/31)	37.8(14/37) *
Target 2	13.6(9/66)	31.7(13/41) *	9.7(3/31)	35.1(13/37) *

Notes: Data were described as mean±SE, *p<0.05.
Abbreviations: HbA1c%, glycosylated hemoglobin; FBG, fasting blood glucose; PBG, postprandial blood glucose; TC, total cholesterol; TG, triacylglycerol; LDL-C, low density lipoprotein cholesterol. Target 1, HbA1c%, FBG and PBG are all up to standards. Target 2, TC, TG and LDL-C are all up to standards.

However, the reduction effects were not detected when the baseline FBG was less than 10 mmol/L and the follow-up duration was extended to 78 weeks (Tables S1 and S2). In order to conquer the influence of the COVID-19 pandemic on the follow-up duration, the follow-up duration was divided into four periods for analysis, which shows that the intervention on blood glucose (HbA1c%: 9.2 vs 8.1, p = 0.020; FBG mmol/L: 8.6 vs. 7.0, p = 0.049; non-intervention vs intervention) and lipid (LDL-C mmol/L: 2.3 vs. 1.8, p = 0.044) may be restricted to moderate length of follow-up durations (between 4 and 12 weeks), rather than short durations (less than 4 weeks) and long durations (more than 12 weeks) (p > 0.05 for blood glucose and lipid indexes) (Table S3).

Discussions

This study provides evidence that the new multidisciplinary pharmacist-clinician model is well suited for managing complex diabetes, specifically among AMI patients with DM. The results show that this model is effective in controlling blood glucose and lipid profiles, with significant improvements observed in FBG, PBG, HbA1C, TC, LDL-C, non-HDL-C, and sd-LDL-C.

The pharmacists' intervention was found to exert more favorable effects in those with higher baseline blood glucose patients and restricted to moderate follow-up durations. Although no significant differences were found in lipid levels between intervention and non-intervention groups, the intervention group had a higher control rate of blood lipid. This model has the potential to make blood glucose and lipid control more achievable for complex diabetic patients.

Glycemic disorders, including diabetes, stress hyperglycemia, and impaired glucose tolerance, are highly prevalent and prognostically important in AMI patients.[22–24] These disorders have been shown to increase mortality during the acute phase of AMI and in the long term, highlighting the need for better therapeutic strategies.[2] Previous studies have mainly focused on admission and in-hospital glucose management after AMI.[25,26] However, the average chronic glucose level, especially the HbA1C value, is another critical factor in the management of AMI patients.[27] A scientific statement from the American Heart Association has demonstrated that a 1-unit increase in HbA1C in diabetic patients increases the risk of macrovascular disease (MI, stroke, or peripheral arterial disease) by 18%, and attaining a target of HbA1C <7% reduces CVD risk by 37% over 11 years.[4] Considering the detrimental effect and high occurrence of hypoglycemia in AMI patients, the glycemic goals should be set to less stringent levels. For example, an HbA1C less than 8.0% is a suitable target in these complex diabetic patients.[18] Our previous study has already shown that pharmacist intervention comprehensively improved glucose control and glucose fluctuation in hospitalized complex diabetic patients.[15] In this

study, we verified that the new pharmacist intervention model resulted in more ideal blood glucose levels (HbA1C, FBG, and PBG) and made achieving blood glucose targets more manageable in the follow-ups. Further, we found pharmacist intervention's effects on blood glucose were more effective in patients with higher baseline FBG levels and moderate follow-up durations (mainly 4–12 weeks in this study). The exact reason for this phenomenon remains uncertain, and we speculated that patients with higher baseline levels are more likely to need multidisciplinary pharmacist intervention. At the same time, the effects of this intervention gradually waned as subsequent blood glucose control improved.

The incidence of dyslipidemia in patients with diabetes can be as high as 42%.[28] Dyslipidemia in diabetes is mainly characterized by elevated TG, elevated LDL-C, and decreased HDL-C levels.[29] Dyslipidemia is believed to be associated with vascular outcomes.[30] Research shows that elevated LDL-C worsens vascular impairment and endothelial function. A previous meta-analysis, including 18,686 diabetic patients, reported that a 1 mmol/L reduction in LDL-C produced a significant 23% reduction in the 5-year incidence of MACEs, regardless of the initial LDL-C level.[31] Non-HDL-C, derived by subtracting HDL-C from total cholesterol, can be used as an alternative to LDL-C, particularly in people with DM.[32] Bhuvana Sunil et al[29] suggested that an increase of 30 mg/dL in non-HDL-C was associated with an increase in the severity of atherosclerotic lesions. Although the clinical benefits of treatment of high TG and low HDL-C levels are still controversial, some studies recommend TG-lowering therapies as an add-on to statin treatment.[30,32] According to the guideline for the prevention and treatment of T2DM in China,[19] comprehensive treatment of diabetes should include blood glucose, lipid profile, blood pressure, and body weight. For lipid management, the lipid targets mainly include TC, TG, and LDL-C. Therefore, in our study, we evaluated not only the changes in actual lipid values but also assessed the lipid targets tailored to DM patients with AMI. We found that blood lipid targets were more easily achievable after the intervention of the new model. Although only follow-up duration restricted to 4–12 weeks, a significant difference was identified in the changes in LDL-C value rather than other parameters on the lipid profile, and the potential lipid management improvements in this model are still worthy of further studies.

In this study, we applied the new multidisciplinary model of glucose management that involves collaboration between clinical pharmacists and clinicians for over two years, as previously reported in our studies.[15,16] Clinical pharmacists play a vital role in clinical medication and patient management, and they can serve as an important complement to clinicians, addressing their lack of time, perceived lack of receptivity, and knowledge gaps in specific drugs.[15] Our study has further demonstrated the significant benefits of this model in blood glucose and lipid management during follow-up. The model involves close collaboration between clinical pharmacists and clinicians, making it an ideal choice for transitioning from drug-oriented to patient-centered care, with the aim of promoting rational drug use and improving the quality of medical services.

One of the main strengths of our study is that we were able to demonstrate the sustained benefits of our blood glucose management model in complex diabetic patients during follow-up visits. Another strength is that we used propensity score matching to reduce the impact of confounding factors,[15] resulting in two comparable groups of 42 patients each. In order to further examine the robustness of the results to violations of the propensity score matching, we also perform a sensitivity analysis, mainly using subgroup analysis based on FBG levels, which is a key impact confounding factor in this study. However, our study also has some limitations. Firstly, due to the impact of the COVID-19 pandemic, follow-up duration was irregular, leading to a higher deviation and lower follow-up rate in this study. To address the possible influence of follow-up times on the results, we further divided follow-up durations into four segments for subgroup analysis. Secondly, although hypertension and obesity are both important factors in comprehensive diabetes management, we were not able to obtain complete follow-up records on these parameters. Additionally, as noted in our previous study, this was a single-center study with a relatively small sample size and limited scope. Future studies with better-designed interventions, more comprehensive follow-up indicators, and larger sample sizes are needed to confirm the benefits of our new model.

Conclusions

This study provides further validation for the beneficial effects of the novel blood glucose management model coordinated with clinicians and pharmacists in follow-ups, particularly for complex diabetic patients. The implementation of this model has shown to improve the achievement of blood glucose (HbA1C, FBG, and PBG) and lipid profile (TC, TG, and LDL-C) targets. Our research is timely given the international attention to healthcare reform, integrated

clinicians and pharmacists, and the need for effective and efficient management models for complex chronic diseases, especially those with cardiovascular complications. The novel management model evaluated in this study has addressed these challenges and holds as a potential viable approach for blood glucose and lipid control. However, successful implementation at other sites and application to other chronic diseases would be necessary to enable translation.

Key Messages

- Hyperglycemia and dyslipidemia can have negative effects on patients who have both diabetes and acute myocardial infarction (AMI). In a previous study, we found that the involvement of clinical pharmacists improved patients' blood glucose levels and fluctuations during hospitalization.
- In this study, we have further demonstrated that clinical pharmacist intervention can lead to long-term improvements in blood glucose and lipid levels in patients with diabetes and AMI. Our innovative model, which combines the expertise of pharmacists and clinicians, offers a practical and effective approach to managing individuals with diabetes and AMI in urban areas. This approach has the potential to make a significant contribution to improving patient outcomes in this population.

Data Sharing Statement

The raw data supporting the conclusion of this article will be made available by the authors to related qualified researchers.

Ethics Approval and Consent to Participate

This study protocol was approved by ethics committees of Renji Hospital, School of Medicine, Shanghai Jiaotong University (KY2019-076). We confirmed that the study complied with the Declaration of Helsinki.

Consent for Publication

Consent for personal data publication was obtained from the participants and their parents or their grandparents.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas. Li, and Gu are the guarantors of the entire manuscript. Shi, Yu, and Shen took part in drafting, revising or critically reviewing the article and gave final approval of the version to be published; Xu and Jiang contributed to the data acquisition, analysis, and interpretation. Lin contributed to supervised the investigation and revised the manuscript.

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work.

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Disclosure

Fang-Hong Shi, Bin-Bin Yu and Long Shen are co-first authors for this study. The authors have declared no conflicts of interest for this article.

References

1. Sun H, Saeedi P, Karuranga S, et al. IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes Res Clin Pract*. 2022;183:109119. doi:10.1016/j.diabres.2021.109119
2. Milazzo V, Cosentino N, Genovese S, et al. Diabetes mellitus and acute myocardial infarction: impact on short and long-term mortality. *Adv Exp Med Biol*. 2021;1307:153–169. doi:10.1007/5584_2020_481
3. Gholap NN, Achana FA, Davies MJ, Ray KK, Gray L, Khunti K. Long-term mortality after acute myocardial infarction among individuals with and without diabetes: a systematic review and meta-analysis of studies in the post-reperfusion era. *Diabetes Obes Metab*. 2017;19:364–374. doi:10.1111/dom.12827
4. Joseph JJ, Deedwania P, Acharya T, et al. Comprehensive management of cardiovascular risk factors for adults with type 2 diabetes: a scientific statement from the American Heart Association. *Circulation*. 2022;145:e722–e759. doi:10.1161/cir.0000000000001040
5. Del Valle KL, McDonnell ME. Chronic care management services for complex diabetes management: a practical overview. *Curr Diab Rep*. 2018;18:135. doi:10.1007/s11892-018-1118-x
6. Ishihara M, Kojima S, Sakamoto T, et al. Acute hyperglycemia is associated with adverse outcome after acute myocardial infarction in the coronary intervention era. *Am Heart J*. 2005;150:814–820. doi:10.1016/j.ahj.2004.12.020
7. Poznyak A, Grechko AV, Poggio P, Myasoedova VA, Alfieri V, Orekhov AN. The diabetes mellitus–atherosclerosis connection: the role of lipid and glucose metabolism and chronic inflammation. *Int J Mol Sci*. 2020;21:1835. doi:10.3390/ijms21051835
8. Schofield JD, Liu Y, Rao-Balakrishna P, Malik RA, Soran H. Diabetes dyslipidemia. *Diabetes Therapy*. 2016;7:203–219. doi:10.1007/s13300-016-0167-x
9. Lewington S, Whitlock G, Clarke R, et al. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. *Lancet*. 2007;370:1829–1839. doi:10.1016/s0140-6736(07)61778-4
10. Hegele R, Ginsberg H, Chapman M, et al. The polygenic nature of hypertriglyceridaemia: implications for definition, diagnosis, and management. *Lancet Diabetes Endocrinol*. 2014;2(8):655–666. doi:10.1016/s2213-8587(13)70191-8
11. Fulcher J, O'Connell R, Voysey M, et al. Efficacy and safety of LDL-lowering therapy among men and women: meta-analysis of individual data from 174,000 participants in 27 randomised trials. *Lancet*. 2015;385:1397–1405. doi:10.1016/s0140-6736(14)61368-4
12. Baigent C, Blackwell L, Emberson J, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. *Lancet*. 2010;376:1670–1681. doi:10.1016/s0140-6736(10)61350-5
13. Martínez-Mardones F, Fernandez-Llimos F, Benrimoj SI, et al. Systematic review and meta-analysis of medication reviews conducted by pharmacists on cardiovascular diseases risk factors in ambulatory care. *J Am Heart Assoc*. 2019;8:e013627. doi:10.1161/jaha.119.013627
14. Alshehri AA, Jalal Z, Cheema E, Haque MS, Jenkins D, Yahyouche A. Impact of the pharmacist-led intervention on the control of medical cardiovascular risk factors for the primary prevention of cardiovascular disease in general practice: a systematic review and meta-analysis of randomised controlled trials. *Br J Clin Pharmacol*. 2020;86:29–38. doi:10.1111/bcp.14164
15. Shi FH, Shen L, Yue J, et al. Intervention by clinical pharmacists can improve blood glucose fluctuation in patients with diabetes and acute myocardial infarction: a propensity score-matched analysis. *Pharmacol Res Perspect*. 2021;9:e00725. doi:10.1002/prp2.725
16. Shi FH, Shen L, Pan MM, et al. The SUCCESSFUL RAPID ADJUSTMENT OF BLOOD GLUCOSE IN A PATIENT WITH ACUTE CORONARY SYNDROME, RENAL INSUFFICIENCY, AND DIABETES: A CASE REPORT OF MANAGEMENT COORDINATED BY CLINICAL PHARMACISTS AND CLINICIANS. *Front Pharmacol*. 2020;11:756. doi:10.3389/fphar.2020.00756
17. Chinese Endocrinologist C. M. D. A. iEgobgmfC. Expert consensus on blood glucose management for Chinese inpatients. *Chin J Endocrinol Metab*. 2017;33:1–10. doi:10.3760/cma.j.issn.1000-6699.2017.01.001
18. Society CD, Endocrinology CSo. Expert consensus on glycated hemoglobin A1c targets and management algorithm for Chinese adults with type 2 diabetes mellitus. *Chin J Diabetes Mellitus*. 2020;12:1–12 doi:10.3760/cma.j.issn.1674-5809.2020.01.001.
19. Society CD. Guideline for the prevention and treatment of type 2 diabetes mellitus in China (2020 edition). *Chin J Diabetes Mellitus*. 2021;13:315–409. doi:10.3760/cma.j.cn115791-20210221-00095
20. Yihong S, Kang C, Xin C, et al. Expert consensus on the management of diabetic patients with cardiovascular diseases. *Chin J Intern Med*. 2021;60:421–437. doi:10.3760/cma.j.cn112138-20201208-00999
21. Shi FH, Yue J, Jiang YH, et al. Sodium-glucose co-transporter 2 inhibitors use improves the satisfaction with anti-diabetic agent treatment: a questionnaire-based propensity score-matched study. *Front Pharmacol*. 2022;12:787704. doi:10.3389/fphar.2021.787704
22. Ertelt K, Brener SJ, Mehran R, Ben-Yehuda O, McAndrew T, Stone GW. Comparison of outcomes and prognosis of patients with versus without newly diagnosed diabetes mellitus after primary percutaneous coronary intervention for ST-elevation myocardial infarction (the HORIZONS-AMI Study). *Am J Cardiol*. 2017;119:1917–1923. doi:10.1016/j.amjcard.2017.03.016
23. Webster K. Stress hyperglycemia and enhanced sensitivity to myocardial infarction. *Curr Hypertens Rep*. 2008;10:78–84. doi:10.1007/s11906-008-0015-0
24. Bartnik M, Malmberg K, Norhammar A, Tenerz A, Ohrvik J, Ryden L. Newly detected abnormal glucose tolerance: an important predictor of long-term outcome after myocardial infarction. *Eur Heart J*. 2004;25:1990–1997. doi:10.1016/j.ehj.2004.09.021
25. Planer D, Witzenbichler B, Guagliumi G, et al. Impact of hyperglycemia in patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention: the HORIZONS-AMI trial. *Int J Cardiol*. 2013;167:2572–2579. doi:10.1016/j.ijcard.2012.06.054
26. Thoegersen M, Josiassen J, Helgestad OKL, et al. The association of diabetes and admission blood glucose with 30-day mortality in patients with acute myocardial infarction complicated by cardiogenic shock. *Eur Heart J Acute Cardiovasc Care*. 2020;9:626–635. doi:10.1177/2048872620925265
27. Marenzi G, Cosentino N, Milazzo V, et al. Acute kidney injury in diabetic patients with acute myocardial infarction: role of acute and chronic glycemia. *J Am Heart Assoc*. 2018;7:e008122. doi:10.1161/jaha.117.008122
28. Li Q. Expert consensus on the prevention and treatment of type 2 diabetes mellitus with dyslipidemia in China. *Chin J Endocrinol Metab*. 2017;33:925–934 doi:10.3760/cma.j.issn.1000-6699.2017.11.004.
29. Sunil B, Ashraf AP. Dyslipidemia in pediatric type 2 diabetes mellitus. *Curr Diab Rep*. 2020;20:53. doi:10.1007/s11892-020-01336-6
30. Goldberg RB, Stone NJ, Grundy SM. The 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guidelines on the management of blood cholesterol in diabetes. *Diabetes Care*. 2020;43:1673–1678. doi:10.2337/dci19-0036

31. Kearney P, Blackwell L, Collins R, et al. Efficacy of cholesterol-lowering therapy in 18,686 people with diabetes in 14 randomised trials of statins: a meta-analysis. *Lancet*. 2008;371:117–125. doi:10.1016/s0140-6736(08)60104-x
32. Mach F, Baigent C, Catapano A, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J*. 2020;41:111–188. doi:10.1093/eurheartj/ehz455