The Effects of Low-Carbohydrate Diet on T2DM Patients in China

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Abstract. T2DM is caused by a complicated interaction between genes, environment, and additional risk factors like obesity and sedentary behavior. LCD is a dietary pattern that strictly limits carbohydrate consumption and increases protein and fat intake. Many previous studies have suggested that this dietary pattern can treat T2DM. This article summarizes the views of many trials, particularly those conducted in China, summarizes the advantages and disadvantages of LCD for the T2DM treatment. Using this dietary pattern can help patients lower HbA1C, lower blood glucose, stabilize the usage of exogenous insulin, lose weight, lower triglyceride levels and raise HDL-C levels. Moreover, depression levels are reduced when nuts are consumed to compensate for the lack of energy from low carbohydrates. On the other hand, controversy remains over this diet for T2DM. Increased LDL-C levels and abnormal intestinal flora are possible adverse effects of this diet. This diet is considered more difficult to adhere to because of the difficulty of satisfying the patient's appetite with small amounts of carbohydrates. This article also suggests directions for subsequent research.

Keywords: T2DM, Low-Carbohydrate Diet, Dietary Pattern.

1. Introduction

Diabetes mellitus (DM) and its effects are a significant global public health issue that affect almost all populations. So far, the prevalence of diabetes in China continues to grow. Guidelines for the Prevention and Treatment of Type 2 diabetes in China (2020 Edition) state that, according to the WHO standards, the findings of a countrywide study conducted between 2015 and 2017 revealed that the prevalence of diabetes among adults over the age of 18 in China was 11.2%. Among them, the prevalence of men is higher than that of women, and type 2 diabetes (T2DM) accounts for more than 90 percent of the total number of Chinese people with the disease [1]. At present, the control of diabetes is mainly through diet, drugs and exercise, among which diet is the basis for the control of various types of diabetes. Low-carbohydrate diet (LCD) is a dietary pattern that strictly limits carbohydrate consumption and increases protein and fat intake. Some studies believe that this dietary pattern can effectively reduce the risk of T2DM and stabilize blood glucose by reducing carbohydrate intake. It is considered as a good dietary pattern for treating diabetes.

This article mainly takes the LCD as the starting point to study the impact of this dietary pattern in the treatment of T2DM, briefly introduces the current status of T2DM and dietary therapy in China, summarizes the recent views on LCD for the treatment of this disease. It will also analyze the impact of LCD on Chinese patients with T2DM in terms of blood glucose, use of exogenous insulin, BMI, lipids, depression, and existing controversies. It will contribute to the study of dietary therapy for T2DM.

2. T2DM

2.1. Definition

DM is associated with chronic hyperglycemia and impaired carbohydrate, lipid, and protein metabolism. The reason is either a disruption in insulin secretion or a disruption in insulin effect, or both. There are two common types of diabetes, T1DM, which generally results from congenital insulin deficiency, and T2DM, which is mostly due to acquired causes. T2DM is caused by a

complicated interaction between genes, environment, and additional risk factors like obesity and sedentary behavior. It is a dangerous and prevalent chronic disease. Complications of diabetes are more life-threatening for patients, people with T2DM tend to have higher mortality rates and higher rates of cardiovascular disease (CVD), acute myocardial infarction, ischemic stroke than the general population mortality [2].

2.2. Current Status of T2DM Prevalence

T2DM is a global disease with a high morbidity and mortality rate that affects people around the world. It not only keeps a stable increase in most developed countries, but also has a rapid growth in developing countries. Due to its large population base and rapid economic development, China has become a country with a high prevalence of diabetes. According to the guideline mentioned above, the population with diabetes is concentrated in the more economically developed areas, with more people suffering from the disease in urban than remote regions. A greater chance of acquiring diabetes exists in those who are overweight and obese [1]. The epidemic of diabetes brings a heavy social and economic burden, and seriously threatens the quality of life of Chinese residents.

2.3. Dietary Interventions

In addition to the commonly used medications, such as metformin and acarbose, more and more experts are looking at dietary modifications as an effective treatment for T2DM. Intermittent fasting can replace insulin to some extent as a treatment for T2DM. The Mediterranean diet may have an effect on T2DM-related processes such as anti-inflammatory and antioxidant characteristics, and alterations in intestinal flora. An Online Intervention research found that individuals with T2DM who were designated to a ketogenic LCD diet and style of living at random remote program improved their glycemic control and lost their weight [3].Therefore, dietary interventions play an integral role in the treatment of T2DM.

2.4. Dietary Therapy: LCD

Diabetes prevention investigation has shown that diet structure has a strong influence in preventing the occurrence of T2DM. Epidemiological studies have suggested that dietary patterns can raise or reduce the risk of diabetes. Reliance on refined grains, pork, beef and lamb and various highly processed meats, excessive alcohol consumption, and quoting sugary beverages may lead to diabetes. Replacing refined grains with whole grain cereals and legumes and beans, eating more vegetables and fruits, and dairy products have the reverse influence and are not associated with fluctuations in weight. LCD is a scientific dietary pattern, individuals need to consume 30-200 grams of carbohydrates per day, or make up for the lack of energy from less carbohydrates by eating more fat and protein, so that carbohydrates account for less than 45 percent of total daily calories (Fig. 1) [4].

A staple food/meal is mean a food rich in carbohydrates, and the three main types in China are steamed buns, noodles, and rice. Hence a low-carb diet means limiting the intake of these foods.

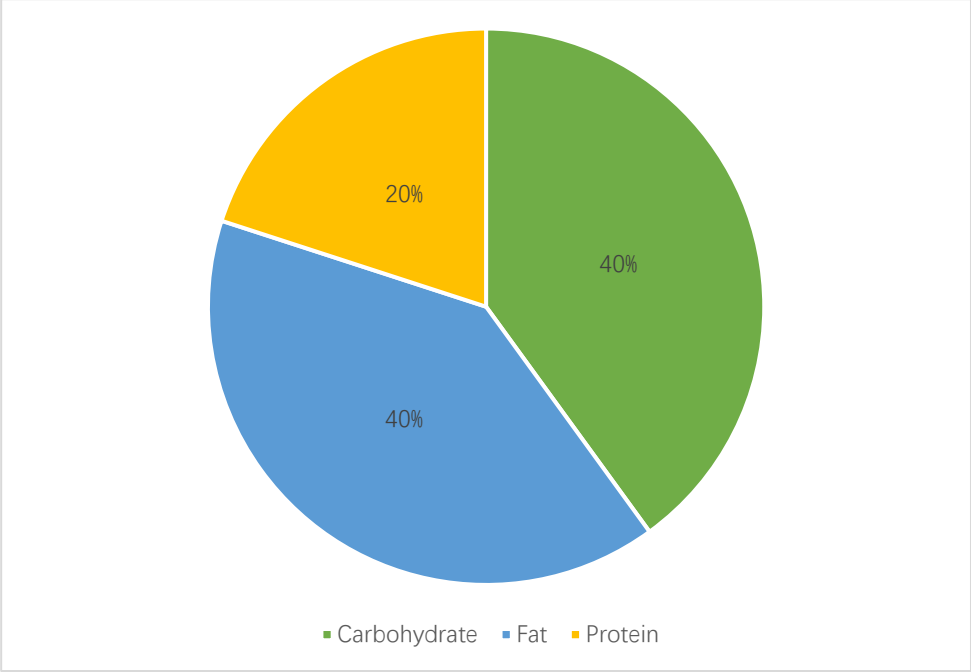


Fig. 1 The proportion of the three energy-supplying substances in LCD

3. Beneficial Effects of LCD on Chinese Patients

3.1. Decreased Levels of Glucose in the Blood

There are several indexes to estimate blood glucose situation. In addition to the well-known fasting and two-hour postprandial blood glucose, HbA1c is also a form of blood glucose measurement. The HbA1c test is the gold standard test for assessing glycemic control, and it has been highly valued in large-scale clinical studies of diabetes complications all over the world.

Having LCD for a long term will decrease HbA1c levels, improving blood glucose. A study recruited participants who were able to communicate, were on their middle-aged or elderly, had been diagnosed with T2DM, and had not changed their use of insulin or oral antidiabetic medications in the month prior to the intervention. This study's findings demonstrated that the LCD group's HbA1c levels significantly decreased. HbA1c values in the LCD group reduced considerably as the starting point (Fig. 2). It means individuals who consumed only 50 grams of staple foods in one meal per day had lower HbA1c levels. Their blood glucose has been controlled dramatically by using LCD [5]. As a result, patients' blood glucose levels will drop if they stick to an LCD for an extended period of time.

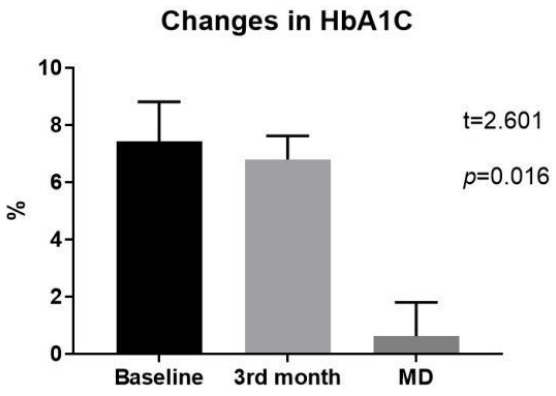


Fig. 2 Changes in HbA1C (%) [5]

3.2. Decrease in Exogenous Insulin Usage

The LCD can help T2DM patients decrease insulin doses, which is used to compensate for the lack of insulin. The most effective hypoglycemic medication, insulin, is required to prolong the lives of patients with severe hyperglycemia. However, it is necessary to pay attention to its side effects. Improper use of insulin and sulfonamides is a significant cause of hypoglycemia. As a common cause of death in older people with T2DM, episodes of hypoglycemia are sometimes more deadly than hyperglycemia. Injected insulin causes hypoglycemia and weight gain, against the T2DM treatment. Therefore, avoiding the use of such medications is a vital component of treating T2DM.

From the research mentioned above, compared to the starting point, after up to three months of LCD treatment, the patient's exogenous insulin use was significantly reduced (Fig. 3). Therefore, controlling carbohydrate intake can effectively help patients reduce the risk of hypoglycemia [5].

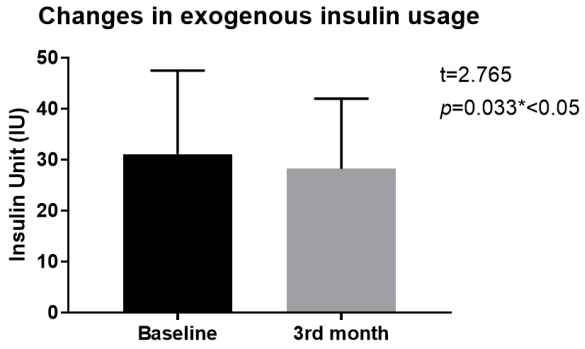


Fig. 3 Changes in exogenous insulin usage (IU) [5]

3.3. BMI Improved

Obesity is a significant contributor to the occurrence of hypertension, CVD, and stroke. These risks are much higher when obesity is associated with T2DM. Meanwhile, it is also a major reason contributing to T2DM and impeding glycemic control. A high-protein LCD is made by lowering the total carbohydrate intake, which makes glucose insufficient for energy supply. This enhances hepatic glycogenolysis and enhances gluconeogenesis, resulting in an improvement in total circulating free fatty acid content. Fatty acids are a very critical source of energy, which can produce more ketone bodies and thus play a full range of roles related to weight loss and body fat reduction. A large number of domestic and foreign experiments have proved that LCD is beneficial for patients to control body weight and improve BMI for T2DM patients.

Among these studies, a trial conducted at the Fourth People's Hospital in Hengshui, Hebei Province, China, treated patients with an LCD+ biguanides and limited total calories to 1,980 kcal/d. As Table 1 shows, the weight of patients decreased with an average weight loss of 1.8 kg/month; at 6 and 12 months of treatment, the body mass of patients increased slightly compared with that at 3 months of treatment, with an average increase of 0.21 kg/month, but still decreased by an average of 3.4 kg compared with that before treatment [6].

Moreover, a trial conducted at Changhai Hospital showed that in obese T2DM patients after metabolic surgery, LCD was effective in reducing patients' weight (weight difference Z=2.31, P&It; 0.05), improving their BMI (BMI difference Z=2.36, P&It; 0.05), and reducing the rate of weight regain (P&It; 0.05) [7].

Table 1. Change in Weight [6]

Experimental period	Weight (kg)
Baseline	93.5±16.2
3rd month	88.2±15.7
6th month	89.2±14.8
12th month	90.1±14.4

3.4. Reduced Triglycerides and Increased HDL Cholesterol (HDL-C)

After taking food, excess sugar will be stored in the form of fat by transformation, which can improve the level of total cholesterol (TC) in the body. Restricting carbohydrate intake avoid excessive sugar stored in the body, interfering with blood lipid levels accordingly [8]. Total cholesterol too high will lead to atherosclerosis, coronary heart disease, hypertension. Some trials have suggested that LCD can reduce the total fat content of patients, but others have found no significant difference in their results. Therefore, the changes in total fat content of patients are not summarized here.

Elevated triglyceride levels may be an indicator of CVD, according to epidemiologic and clinical investigations. Genetic evidence from various studies supports these findings, suggesting that triglycerides (TG) and TG-rich lipoproteins may exert similar pathogenic effects with LDL cholesterol (LDL-C), leading to atherosclerosis and CVD [9]. A meta-analysis showed that interventions using an LCD reduced blood TG levels. Moreover, this report linked LCD to increased HDL-C levels and concluded that LCD could also improve HDL-C concentration in T2DM patients [10]. High levels of HDL-C are effective in preventing CVD. T2DM and HDL-C concentration have a significant impact on the development of CVD. Therefore, increasing HDL-C levels in patients with T2DM is of great importance in preventing diabetic complications and other aspects by using LCD.

3.5. Improve Depression

Compared to older adults without DM, those with DM are more likely to have comorbid depression. According to a meta-analysis, diabetes patients had a much higher prevalence of depression than people without the disease (17.6% vs. 9.8%) [11]. Therefore, treating comorbid depression in older adults with DM presents unique challenges and opportunities for clinicians.

A study conducted at the 1st and 2nd Affiliated Hospitals of Soochow University, by screening adult patients who had T2DM, had no shift in diabetes-related drugs 15 days before the treatment, reported that an almond-based LCD (a-LCD) decreases T2DM patients' depression score. Compared to the baseline (48.41 ± 8.05), the depression score decreased after the intervention (42.07 ± 5.80) (Table 2).

In addition, since there may be a link between depression and human gut microbiota, this study also found that a-LCD dramatically enhanced the relative abundance of short-chain fatty acids (SCFA) producing bacteria Roseburis and Ruminococcus. According to these findings, the capacity of a-LCD to encourage the development of bacteria that generate SCFAs may be connected to its potential to alleviate depression in T2DM patients, which in turn raises SCFA levels and activates GPR43, maintaining GLP-1 production [12].

However, studies from various nations have shown conflicting results about LCD's impact on depression. In addition to ethnic reasons, this may also be related to whether or not high amounts of almonds are added to the diet.

Table 2. Change in depression score [12]

Experimental period	a-LCD(n=22)
Baseline	48.41 ± 8.05
3rd month	42.07 ± 5.80
t	6.196
p	<0.01*

4. Area of Controversy Over LCD for T2DM

Regarding the impact of LCD on the treatment of diabetes, worldwide scientists have similar concerns. A trial involving thousands of people showed that LCD may raise LDL-C levels in patients while reducing weight and lowering blood sugar. They wonder if the benefits of this dietary pattern outweigh the drawbacks [13]. In response to the idea that LCD promotes unrestricted intake of

saturated fats and increase LDL-C levels, some opponents argue that this ignores the many benefits of LCD, such as reducing the risk of CVD.

In addition, diabetes and obesity are associated with inflammation, and the gut microbiota may regulate metabolic endotoxemia, inflammation, and related diseases by increasing intestinal permeability. It has been suggested that LCD reduces the intake of fermentable dietary fiber, which may lead to changes in the gut microbiota and cause metabolic disturbances [14].

Moreover, since LCD is not a regular diet, successful adherence to this dietary pattern becomes one of the obstacles in treatment. In most of the above experiments, there was an unavoidable weight regain and difficulty in adherence in some patients. It was believed that while LCD can reduce fat mass and alleviate T2DM in the short time, the long-term influences are not significant. Due to excessive intake of fat and protein, it may lead to nutritional imbalances and ketosis effects [15].

5. Conclusion

The increasing prevalence of diabetes requires targeted treatments for patients, among which the LCD is a convenient and effective way. It has different effects on T2DM patients in diverse terms. Using this dietary pattern can help patients lower HbA1C, lower blood glucose, and reduce the risk of hypoglycemia by stabilizing the use of exogenous insulin. At the same time, LCD can help patients lose weight to some extent. Since obesity is a major cause of hypertension, stroke and CVD, this will reduce the patient's risk of developing related diseases. LCD has also been shown to lower TG levels and raise HDL-C levels. Moreover, depression levels are reduced when nuts are consumed to compensate for the lack of energy from low carbohydrates. Although LCD has many benefits, controversy remains over this diet for T2DM. Increased LDL-C levels and abnormal intestinal flora are possible adverse effects of this diet. In addition to this, this diet is considered more difficult to adhere to because of the difficulty of satisfying the patient's appetite with small amounts of carbohydrates.

The many long-term complications of diabetes, including microvascular disease and macrovascular disease, are factors contributing to the high mortality rate of diabetes. However, few studies have been conducted on LCD for the treatment of diabetes in patients with these comorbidities, and more studies have been conducted in patients with diabetes with milder symptoms in China. Caution is needed in using LCD in patients with T2DM who already have these comorbidities. In future studies, it is hoped that this population will be more involved. In addition, the human diet is extremely complex and diverse, and studies of diet are often difficult. These studies also suffer from short experimental time and small number of subjects. Due to individual variability, the effects of diet cannot be reflected completely in each individual. This is where that needs to be focused on in future research.

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