



Beneficial Effects of Low Carbohydrate Diet (LCD) with Recently Emerged Solid Evidence

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Abstract

Various discussions have continued concerning low carbohydrate diet (LCD) and calorie restriction (CR). The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) have gradually recognized LCD as the recommendation for nutritional treatment. Recent reports have shown the predominance of LCD with clinical evidence from the accumulated data of the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS), with analyses of total LCD scores (TLCDS). Using TLCDS to analyze 139 thousand person-years, the hazard ratio (HR) of total mortality was 0.87 for TLCDS and 0.76 for vegetable (VLCDS). Authors continue developing LCD activities through the Japan LCD Promotion Association (JLCDPA).

Keywords

Low Carbohydrate Diet, Calorie Restriction, Nurses' Health Study, Total LCD Scores, Japan LCD Promotion Association

Abbreviations

LCD: Low Carbohydrate Diet; CR: Calorie Restriction; NHS: Nurses' Health Study; TLCDS: Total LCD Scores; JLCDPA: Japan LCD Promotion Association

Commentary

For the adequate treatment of diabetes, obesity, hyperlipidemia, and lifestyle-related diseases, various discussions and controversies have been observed concerning low carbohydrate diet (LCD) and calorie restriction (CR) [1,2]. The statement of the American Diabetes Association (ADA) has changed according to the existing evidence. In 2006, LCD was not adopted due to insufficient evidence [3]. After that, the ADA

announced dietary recommendations in 2008, stating that LCD became one of the recommended dietary therapies [4]. LCD has been evaluated and recommended in the US and European countries, but its safety has been debated. According to the ADA statement, LCD has the most evidence for improving glucose variability, and CR and Mediterranean diets can be applied based on patient preference [5]. Successively, the European Association for the Study of

Diabetes (EASD) followed suit [6].

On the other hand, Ebe in Japan first adopted and reported the clinical efficacy of LCD in 2004 [7]. After that, authors and collaborators developed the activities of LCD medically and socially through seminars, textbooks, and medical papers via the Japan LCD Promotion Association (JLCDPA) [8,9]. JLCDPA has continued presenting useful LCD methods, which are super-LCD, standard-LCD, and petite-LCD [10]. In light of a systematic review, LCD data in Japanese diabetic patients were reported by Yamada [11]. Recently, several useful papers have been published about LCD and CR. From this clinical data, the continuing discussion, with various controversies thus far, will be resolved, and the predominance of LCD may be clarified. Some crucial points from these reports will be summarized and presented in this article.

For the latest research on LCD, the relationship between post-diagnosis LCD patterns and the mortality of T2D individuals was investigated. The protocol included participants from the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS), as well as the application of the total LCD score (TLCDS) [12]. Among 139 thousand person-years, 4.6 thousand deaths were observed. As TLCDS shows a 10-point increase, the hazard ratio (HR) for total mortality was 0.87 for TLCDS, 0.76 for vegetable (VLCDS), and 0.78 for Healthy LCDS (HLCDS). Both VLCDS and HLCDS showed significantly lower cardiovascular disease (CVD) and cancer mortality. Each 10% increment of TLCDS, VLCDS, and HLCDS from the pre- to post-diagnosis period showed lower total mortality by 12%, 25%, and 25%, respectively. In conclusion, T2D patients showed moderate adherence to LCD patterns, providing high-quality macronutrients associated with lower total mortality.

The current report from NHS and HPFS in 2023 showed the clinical efficacy of LCD. In contrast, a previous report in 2010 from NHS and HPFS showed opposite results [13]. The different aspects can be analyzed. The characteristic points in the previous report include: i) NHS: female nurses (n=121,700), ii) male medical staff (n=51,529), iii) these are prospective cohorts from 1976 and 1986, iv) applicants

include all cases with and without diabetes. In contrast, the present report includes i) analyzed cases that are all newly-diagnosed with type 2 diabetes (T2D) until 2018, ii) cases who were previously diagnosed with T2D were excluded, iii) cases with previous cancer or cardiovascular diseases were excluded, iv) analyzed data were smaller for females (n=7,224) and males (n=2,877). The conclusion was that the group with fewer carbohydrates showed decreased mortality when cases are limited to T2D [12].

For cardiovascular risk, the benefit of LCD was studied in a prospective study. The protocol included 5,677 cases, and they were followed up for 6.3 years, totaling 39,401 person-years with 1,432 deaths during the period [14]. After adjustment for HbA1c and lifestyle factors, the third quartile of the overall LCD score showed the lowest risk for mortality with an HR of 0.65. The multivariable-adjusted HR for mortality was 1.00, 0.78, 0.73, and 0.74 in the first to fourth quartiles, respectively. When replacing 2% of energy from carbohydrates with polyunsaturated fatty acids (PUFA) or plant-based protein, total mortality decreased by about 23% to 37% with clinical efficacy. Consequently, HLCDS showed a significant relationship with decreased mortality in T2D adults. By continuing a well-balanced LCD, such as PUFA or plant-based protein, premature death in T2D may be prevented.

Regarding the long-term efficacy of LCD on mortality, the quality and source of carbohydrates have been investigated in a prospective cohort study. The protocol included 20,206 cases (including 13.8% with diabetes), and vegetable- and meat-based LCD scores were calculated for hazard ratios (HRs) [15]. Concerning the data from the highest vs. lowest quartiles, vegetable-based LCD showed HRs of 1.16 and 1.30 for all-cause and CVD mortality, respectively. In contrast, meat-based LCD showed HRs of 0.89 and 0.81 for the same outcomes. The detailed carbohydrate content ratios in Quartile 1 vs. 4 were 67.6% vs. 46.5% in total LCD scores, 60.9% vs. 52.2% in vegetable LCD scores, and 65.9% vs. 48.0% in meat LCD scores. Thus, vegetable-LCDS was positively associated, and meat-LCDS was negatively associated with both mortality outcomes in elderly Asian people.

In the latest report, a newly introduced smoothie with modified carbohydrate content (SMMC) was compared with the standard diabetes-specific nutritional formula (DSNF) in terms of glucose variability, insulin response, and lipid changes for patients with obese type 2 diabetes (T2D) [16]. SMMC showed a significantly lower glucose response, associated with lower insulin, C-peptide, and NEFA responses, and a higher glucagon response. It may have a unique composition of carbohydrates, fats, and amino acids in the current smoothie, associated with several positive effects.

Regarding metabolic-dysfunction-associated fatty liver disease (MAFLD), a comparison study was conducted on LCD and CR. The study included 3,961 adult cases, and the relationship between MAFLD and LCD/CR scores was analyzed [17]. As a result, cases in the highest tertile of healthy LCDS (0.63) or healthy CR score (0.64) showed a lower risk of MAFLD. In addition, cases with unhealthy CR scores in the second and third tertiles showed 49% and 77% higher risks of MAFLD, respectively. Thus, healthy LCD and CR showed protection against MAFLD, however, unhealthy CR may increase the risk of MAFLD. Both the quality and quantity of macronutrients possibly influence MAFLD development.

As mentioned above, LCD seems to show clinical predominance compared to CR in recent reports with medical evidence. Authors will continue various activities concerning LCD and hope that LCD will provide people and patients with physical, psychological, and social benefits in the future.

Conflict of Interest

The authors have read and approved the final version of the manuscript. The authors have no conflicts of interest to declare.

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