The Low-Carbohydrate Diet as an Effective Measure to Achieve Significant Weight Loss and Improve Parameters of Cardiovascular Disease

A Literary Review

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Introduction

The World Health Organization (WHO) defines the terms overweight and obesity as "the abnormal or excessive fat accumulation that presents a risk to health." Furthermore, obesity is described as the result of energy imbalance between energy consumption and expenditure. WHO underlines the observation of increased intake of foods that are dense in energy and high in fat globally (1).

According to the WHO, worldwide obesity has almost doubled since the 1980s. 35 % of people aged ≥20 were in 2008 overweight, and 11 % could be characterized as obese. Numbers are well matched for the prevalence in Norway (2). The classification of overweight and obesity in Body Mass Index (BMI) for adults is as follows:

Overweight:	≥ 25.0
Pre-obese state:	25.0-29.9
Obese:	≥ 30.0
Obese class I:	30.0-34.9
Obese class II:	35.0-39.9
Obese class III:	≥40.0

Overweight and obesity in adults are associated with increased risk of type II diabetes, cardiovascular disease (CVD) and certain types of cancer (1, 3). Mental health can also be unfavourably affected (2).

CVD is the most common cause of death in Norway, and is the reason for approx. 35 % of all deaths every year according to a rapport published in 2010 (2). Furthermore, 15 % over 15 years of age, and 43 % over 75 years of age have CVD. According to the same rapport, the most important risk factors for CVD include a diet consisting of high intake of saturated fat and salt, overweight and obesity, and lastly tobacco and a sedentary lifestyle.

In Norway, there has been a great interest in the Atkins/Low-Carbohydrate (LC) diet. This has sparked much debate, due to the extremely conflicting nutritional recommendations presented by

the government versus the nutritional approach of the Atkins LC diet (4). The debate is largely about the safety of a diet encouraging such a liberal intake of fat, and the possible unfavorable effects it may have on CVD risk.

Helsedirektoratet promotes a diet consisting of 25-35% fat, 10-20 % protein and 50-60 % carbohydrates which are comparable to those in other countries, for instance the USA with 45-65:10-35:20-35 % of COH:Prot:Fat respectively (5): it is further explained that this nutritional approach suits the needs of a healthy and sick population with a good basic nutritional status, that are not at risk of undernourishment. Furthermore, it is also the recommended diet for people with diabetes, CVD and overweight, but acknowledges that it may be necessary with individual adjustments. It is important to underline that the government guidelines of carbohydrate intake discourages great intake of refined sugars, and that carbohydrates in the form of whole grains is to be preferred over processed, refined carbohydrates. Vegetables and fruits (also containing carbohydrates like potatoes etc.) are strongly encouraged. This dietary approach has been associated with reduction in mortality among high risk patients and is generally supported by studies to have advantageous effects on CVD risk (6,7).

To better understand the conflict of this debate, it is necessary to look at the specifics of the nutritional recommendations of the Atkins Diet. This is all found in Dr. Atkins book *Dr. Atkins' New Diet Revolution*, and is explored below.

What is The Atkins Diet?

Since Dr. Atkins first published his book Dr. Atkins Diet Revolution in 1972, it has been debated whether this LC diet is a healthy approach to weight loss. Much has been said about Dr. Atkins, who himself followed this diet, and whether he in the end died of his own diet; it has been claimed that he had a history of myocardial infarction, heart failure and hypertension, but these claims have also been denied. However, even if it were not true, many have been interested to explore whether this diet is a viable option to the conventional Low-Fat (LF) diet, which is the officially recommended dietary approach today to achieve weight loss. Many are concerned about the promotion of liberal intakes of fats, among them saturated fats, and the possible detrimental effects in regards to cardiovascular risk in subjects consuming this diet (8). Research suggests that an

increase in dietary fat increases the concentration of coagulation factor VII, and hence elevates the risk of thrombosis, myocardial infarction and cerebral thrombosis (8). Traditionally, the recommendation has been to cut down on saturated fats (9). This is now being challenged by ever newer research. In a recent meta-analysis of prospective epidemiologist studies, the authors concluded that there was no significant evidence that saturated fat was associated with increased risk of coronary heart disease (CHD) and CVD (10).

While the studies in this review were conducted on subjects with no known cardiovascular disease, concern has been expressed in regards to this diet particularly if used on patients with CVD, diabetes type II, dyslipidaemia and/or hypertension, due to the fear that it can lead to enhancement of already abnormal metabolic function (11).

However, regardless of current research, the diet has been, and continues to be popular. The book has sold millions of copies, and is one of the most used dietary approaches for weight loss in the world. Despite the expressed concerns, Atkins argues fiercely that the LC nutritional approach is a much more healthy and viable option than the recommended LF diet for anyone who wishes to lose weight.

The Atkins diet supposedly "keeps lost pounds off forever" and “keeps you slim and healthy and helps you stay that way" (12). These are some of the many things Atkins promises in his book. But what is the Atkins diet and does it really do what it promises? What makes it different from other diets, and is it more effective than the conventional LF diet?

The LC diet described in the book dictates an extremely low-carbohydrate diet, consisting of four phases, where the consumer will increase his or her daily intake of carbohydrates up to a point where he/she no longer loses or gains weight. The regime is as follows:

1. Induction phase: This is a phase which lasts for a minimum of 2 weeks, and can safely be used for six months or longer. In this phase, the consumer cannot consume more than 20 g of carbohydrates per day, and some things are absolutely forbidden. According to Atkins, this extremely low carbohydrate intake will change the body ´s metabolism - from normally using carbohydrates/sugar as the main source of fuel and energy, the body is forced to use fat and fat storages. This state is called lipolysis/ketogenesis, and is the result of the fact that there are no

available carbohydrates to use for fuel. When COH intake is low enough, the body produces ketone bodies; these are waste products and can be measured in urine to assess diet adherence.

2. On-going Weight Loss phase (OWL): The consumer is allowed to add 5 grams of carbohydrates every week (5 grams is 1 level, and consumers are encouraged to increase carbohydrate intake by 1 level every week). This continues until the consumer stops losing weight. As long as the consumer stays below the Critical Carbohydrate Level for Losing (CCLW), he/she will lose weight. The consumer goes on to this phase when he/she is 5-10 pounds away from goal/ideal weight.
3. Pre-Maintenance Phase: When the consumer only has 5-10 pounds from ideal weight to lose, additional 10 g of carbohydrates per week is allowed. Weight loss at this point is very slow, often less than a pound each week, but the consumer can continue to add 10 g per week as long as he/she keeps losing. The duration of this phase is usually 2-3 months.
4. Lifetime maintenance: When the consumer has reached his/her ideal weight, the number of carbohydrates when he/she stopped losing (at ideal weight) is the Critical Carbohydrate Level for Maintenance (CCLM). Atkins divides subjects into classes of high and low resistance, depending on how many carbohydrates the subject can eat before he/she gains weight. The amount of carbohydrates tolerated at this point (no weight loss or gain, range of 5 pounds) is the max amount of grams carbohydrate allowed as a lifetime regime. Usually, the amount of COH in grams which is CCLM will be lower than 20 % of total energy consumption.

In contrast to other diets focusing on calories, the Atkins diet stresses the fact that his diet is per say not a calorie-restricted diet, but a carbohydrate restriction diet. This is very different from the more accepted approach for weight loss, where the energy balance (calories consumed, calories used) is the vital and most important factor for weight loss. However, it is a well-known fact that individuals consuming the Atkins diet are known to reduce calories as well, which Atkins acknowledges is a side-effect of the satiety of this particular diet (12). The question about macronutrient composition versus calorie restriction is an interesting one, and raises the question of whether and how important macronutrient composition is when attempting to lose weight. Furthermore, it has also been one of the greatest sources of worry; with a shift in macronutrient distribution, eliminating COH which normally makes up almost half of the energy content of a normal diet, subjects on the Atkins diet must compensate by eating increased amounts of protein and fat. The greatest concern is directed towards whether the increased intake of dietary fat (particularly saturated fat) affects cardiovascular risk factors or not.

Cardiovascular risk factors

When discussing cardiovascular risk factors, one considers weight, serum/plasma cholesterol, High-Density-Lipoprotein (HDL), Low-Density-Lipoprotein (LDL) and triglycerides (TAG); they make up the greatest proportion of this risk profile (13). In addition, blood pressure and insulin/glucose levels also come into consideration.

The recommendations from WHO limit total saturated fat to 10 % of total energy intake, while the American Heart Association (AHA) recommends similarly a fat restriction of 7 % of total energy intake. The Atkins diet (and LC diets in general) challenges these recommendations by allowing an ad libitum approach to fat intake, but only if it replaces carbohydrates, and not in addition to carbohydrates (12). This is the basis of much concern due to the fear of unfavorable changes in cholesterol and TAG.

Increased cholesterol, known as hypercholesterolemia, is a great risk factor for the development of CVD and atherosclerosis (14). Cholesterol is packaged in lipoproteins due to its insolubility in water, and exists mainly in two forms: HDL and LDL. The HDL, also known as the "good" cholesterol, brings cholesterol from the bloodstream, from LDL, and as well as from artery walls to the liver to be disposed of (15). Research has shown that CVD is inversely related to HDL levels (14). LDLs´ role on the other hand is to bring cholesterol from the liver to the rest of the body so that cells can use fat as a source for energy. When LDL particles in the blood stream are in excess, they can form deposits in the artery walls, narrowing them and thus limiting blood flow. Additionally, plaque formation is associated with thrombosis and embolus (15). Thus CVD mortality and morbidity is positively related to LDL concentrations (14).

In a review where 41 studies were included (Cohorts, RCT and International Studies), the authors found a clear association between s-cholesterol and the incidence of ischaemic heart disease (IHD) (16). More specifically, it was found that a decrease in total s-cholesterol in the 10 cohorts of 10 %, which translated into 0.6 mml/l, was directly associated with a decrease of 54 % at age 40 years in the incidence of IHD. Furthermore, the incidence decreased by 27 % at age 60 years, 20 % at 70 years and 19% at 90 years. Similarly, the results from the 3 international studies and the 28 RCTs used in the review were consistent with these results (16).

To rebuke the supposed fallacy that "a nutritional approach that promotes a liberal intake of high-fat meats and dairy products will raise cholesterol levels, ultimately leading to heart disease" (12), Atkins points to recent studies, and mentions in particular a study where 12 (correction: 10 in the article) healthy men followed a LC diet for 8 weeks; at the end of the dietary intervention, the participants had each lowered their TAG levels by 55 % (17). Though this study is both of very short duration (only 8 weeks) and the number of subjects is incredibly small, Atkins fails to mention other aspects of the results of the trial; namely transient increase in LDL and tot-cholesterol, which are two very important CVD risk factors. Atkins repeatedly also points out, that in comparison to a LF diet, the LC diet lowers TAG and increases HDL, and thus is more favorable than the other said diet.

TAG is the most abundant type of fat in our bodies (15). Excess calories are turned into triglycerides and stored in fatty tissues (18). Elevation of triglycerides is known as hypertriglyceridemia, and is associated with increased risk of CVD. While statins are the usual prescribed medication to lower and normalize cholesterol levels, the treatment for hypertriglyceridemia is not as easy. Lifestyle change, in form of a LF diet, especially low saturated fat diet has been the official recommendation as a good measure to treat it (19). Atkins disagrees, suggesting that an LC diet, which has shown to improve TAG levels, is the appropriate diet and serves as a treatment in people with hypertriglyceridemia. It is uncertain how the LC diet affects lipid levels in subjects with already known lipid metabolism disturbances.

In summary, many parameters make up a CVD risk profile. While Atkins certainly argues for the improvement of CVD risk parameters, particularly HDL and TAG, there is much discussion about whether this is a diet which can be recommended on a general basis, and whether the possible unfavorable effects of this diet outweigh the said favorable effects.

The purpose of this review was to therefore explore many of the questions which remain unanswered about the safety of this diet. Can the Atkins diet be used as an effective measure to lose weight, and how does it affect CVD risk factors? It is a well-known fact that with weight loss, CVD risk profile improves - so what benefits does consumption of an Atkins diet provide to the average consumer, if any, compared to the conventional dietary approach for weight loss (low-fat diet)? More importantly, is the research published to date adequate in regards to making educated recommendations in a clinical setting to overweight/obese patients wanting to lose weight?

Hence, appropriate articles after searches in PubMed were selected.

The findings on weight loss and parameters for CVD risk factors were reported as raw data (Table I-IV) and reproduced in tables as per cent change from baseline values (Table V) to get a proper overview and a means of comparison. Lastly, an evaluation of the whether the claims from Atkins based on the published literature can be justified was performed, with an emphasis on whether the LC diet is a viable option to the LF diet in regards to weight loss and whether the already raised concerns regarding increased CVD risk are justified.

Methods

The aim of this review was to go through articles concerning the LC diet based on the Atkins diets and its´ guidelines. The main goal was to summarize the weight loss effects (if any) and additionally look at whether this diet had any significant effects on cardiovascular risk factors.

To find the appropriate articles, where the main parameter was weight loss as a consequence of diet, two search terms were defined. The searches were conducted in PubMed. They were as follows:

1. ((atkins diet) AND weight loss) AND cardiovascular effects)

and

2. ((low carbohydrate diet) AND weight loss) AND cardiovascular effects)

Additionally, LIMIT to only include Randomized Controlled Trials (RCTs) and Clinical Trials was applied

The search warranted 27 and 57 results, respectively. The search was conducted in Aug./Sep. 2012.

The results were all then individually reviewed, and based on the set inclusion/exclusion criteria, the appropriate articles were selected.

The inclusion/exclusion criteria were as follows:

- n > 20 (after dropout)
- The nature of the LC diet had to be properly defined. Only COH intake of < 20 % of total energy consumption per day, or a description and reference to the Atkins diet (with as low as < 30 g/d) were accepted.
- Studies conducted solely on subjects suffering from Obesity Class II and III (BMI > 35) were excluded.
- The duration of the dietary intervention had to last at least 3 months or more.

As the articles were thoroughly explored, so were the references used in these articles. Appropriate articles from the references were then thoroughly reviewed, and the studies that fulfilled the already set inclusion/exclusion criteria (see above), were also included in the final data collection.

Figure I. Flow Diagram showing the inclusion/exclusion of studies after PubMed searches.

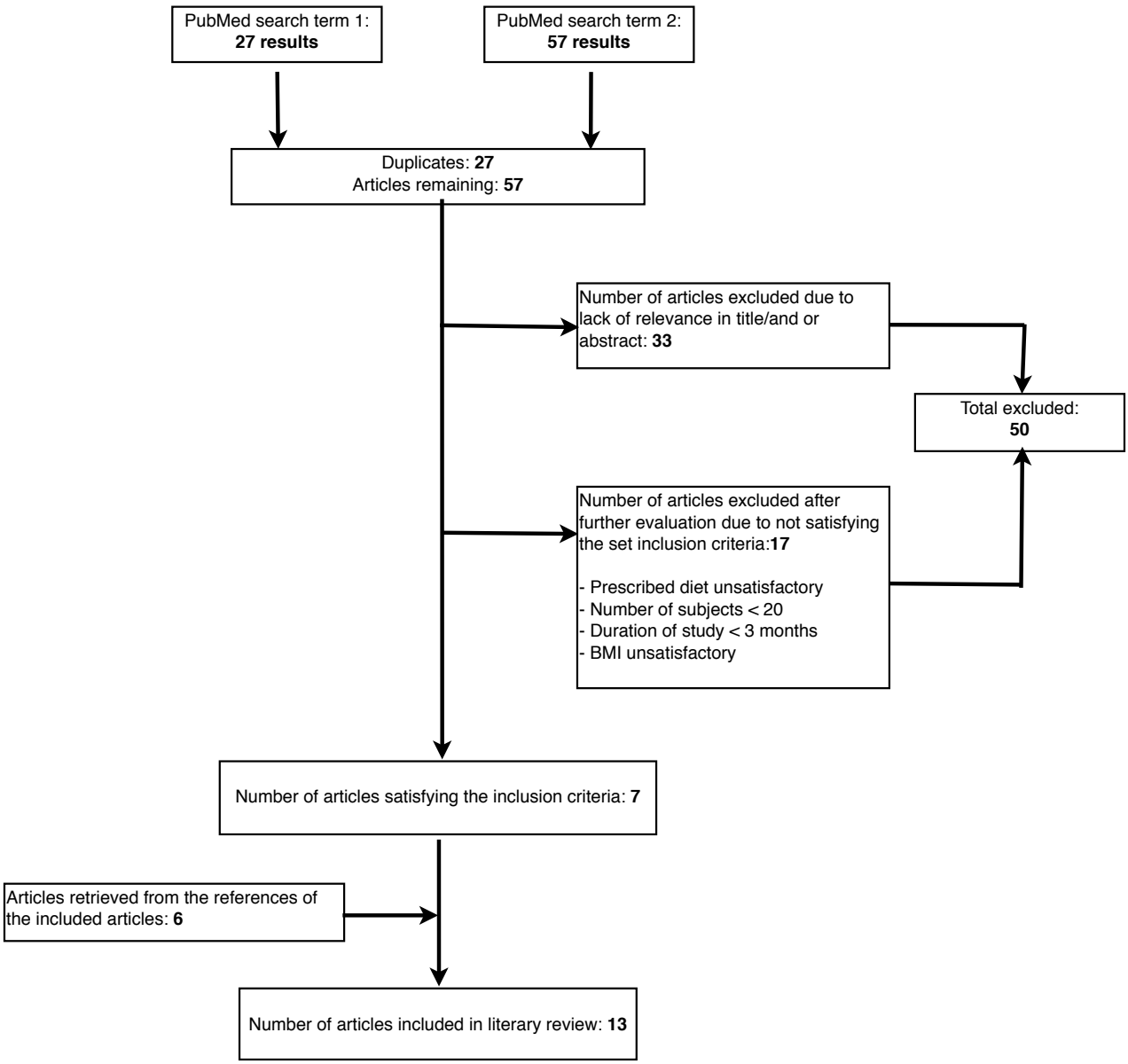

Table I: Overview of studies included.

Study	Number of subjects in LC group	Duration of intervention	Diets compared in study	COH content in LC diet	Energy restriction ?
Foster (2010) [20]	Assigned: 153. Attrition at assessment 3, 6, 12 and 24 months were 9%, 16%, 26% and 42%, respectively.	24 months	LC vs LF	First 12 weeks: COH intake limited to 20 g/d in form of low glycemic index vegetables. After 12 weeks, gradual increase with 5 g/d per week. Participants followed guidelines as described in Dr. Atkins´ New Diet Revolution.	Not for LC.
Wycherley (2010)[21]	Assigned: 57. Analyzed after dropout: 26	12 months	LC-high saturated fat diet vs LF diet	Dietary plan with 4% of total energy from COH. Objective to restrict COH to < 20 g/d for the first 8 weeks, thn increase to < 40 g/d for the remainder of study.	Moderate energy restriction for both diets: 6000 kJ day for women, 7000 kJ day for men.
Lim (2010)[22]	Assigned: 30. 24 completed 12 weeks intervention, 17 completed 15 months intervention, 27 included in analysis	15 months	VLC, VLF, HUF and control group	4 % of energy as COH	Isocaloric diets - restricted to 6500 KJ.
Morgan (2008)[23]	Assigned: 57	6 months	Atkins, Weight Watchers, Slim-Fast, Rosemary Conley, Control	Atkins diet.	Not specified.
Tay (2008)[24]	Assigned: 55 Analyzed after dropout: 45	6 months	VLCHF vs HCLF	4 % of total energy as COH. Restricted to < 20 g/d. Optional to increase COH intake to <40 g/d for the remainin 16 weeks.	Isocaloric diets with a moderate calorie restriction of approx. 30% (6000 kJ for women, 7000 kJ for men).
Brehm (2003)[25]	Assigned: 26 Analyzed after dropout: 22 (7 dropouts)	6 months	VLC vs LF	Max. intake of 20 g COH per day. After 2 weeks, subjects were allowed to increase their intake of COH to 40-60 g/d (but only if continued ketosis).	VLC: Ad libitum. Calorie restriction only for LF diet.
Foster (2003) [26]	Assigned: 33	12 months	LC vs Conventional Diet	Carbohydrate intake limited to 20 g/d for the first two weeks, with gradual increase until stable and desired weight was achieved. Subjects were instructed to follow the Atkins diet - was given a copy of Dr Atkins´New Diet Revolution.	LC: Ad libitum. Coventional Diet: Calorie restriction of 1200 to 1500 kcal per day for women and 1500 to 1800 kcal per day for men
Yancy (2004) [27]	Assigned: 60 Analyzed: 59 Completed intervention: 45	6 months	LC vs LF	COH intake limited to < 20 g/d. Increase of approx. 5 g of COH to daily intake each week when halfway to body weight goal.	LC: Ad Libitum. Calorie restriction only for LF diet.
Gardner (2007)[28]	Assigned: 77 Completed: 68 Primary Analysis: 77	12 months	Atins, Ornish, LEARN and Zone	Atkins: Aimed for COH intake of 20 g/d or less in the induction phase (2-3 months), and 50 g/d or less for the subsequent ongoing weight loss phase.	

Study	Number of subjects in LC group	Duration of intervention	Diets compared in study	COH content in LC diet	Energy restriction ?
Shai (2008) [29]	Assigned: 109 Completed: 85 Primary analysis: 109	24 months	LC, Mediterranean and LF	COH intake limited to 20 g/d for 2-month induction phase, with gradual increase to max 120 g/d.	LC: Ad Libitum. Calorie restriction only for the LF and Mediterreanean diets.
Dansinger (2005)[30]	Assigned: 40 Primary Analysis: 40 Secondary completers anlysis: 21	12 months	Atkins, Zone, Weight Watchers and Ornish	Atkins: Aimed for COH intake < 20 g/d, with gradual increase toward 50 g/d.	Not for LC.
Brinkworth (2009) [31]	Assigned: 55 Withdrawal: 22 Mixed Model Analysis: 55 Completers: 33	12 months	LC vs LF	4% of total energy as COH. Objective to restrict COH to < 20g/d or the first 8 weeks, and then to < 40 g/d for the remainder of the intervention period.	Eergy-restricted isocaloric diets - restricted to approx 6000 kJ/d for women, and approx 7000 kJ/d for men.
McAuley (2005)[32]	Assigned: 31 Withdrawal: 7 Analysed: 24	12 months	LCHF, HP and HC	COH consumption < 20 g/d during the first 2 weeks. Thereafter an increase up to 50 g/d by 8 weeks and continuing thereafter with the amount of COH tht maintained initial weight loss.	

Table II: Results - Weight loss.

Weight (kg)	Foster (2010)	Wycherley	Lim	Morgan	Tay	Brehm	Foster (2003)[1]
Baseline	103.3 (15.5)	94.2 ± 3.2	87.6 ± 2.3	92.1±13.6	94.4±15.5	91.2±8.4	98.7 ±19.8
2 mo				85.1±10.9			
3 mo	-9.49 (-10.1 to -8.85)		-8.0 ±2.8			-7.6±0.7	-6.8 ±5.0
6 mo	-12.18 (-13.1 to -11.2)			83.2±10.6	-11.9 ±6.3	-8.5±1.0	-7.0±6-5
12 mo	-10.87 (-12.1 to -9.67)	-14.9 ± 2.1	-2.9 ± 4.9[2]				-4.4 ±6.7
24 mo	-6.34 (-8.06 to -4.63)						
Percent change (%)	-6.34 (-8.06 to -4.63)	-15.8	- 3.3	-9.7	-12.6	-9.3	-4.4 ±6.7

[1)] Except for baseline values, values are per cent change from baseline (raw data from study)
[2)] Data at 15 months.

Table II. Continued.

Weight (kg)	Yancy	Gardner	Shai	Dansinger	Brinkworth	McAuley
Baseline	98.1 ±15.2	86±13	91.8±14.3	100±14	93.9 ±15.5	97.2±10.4
2 mo				-4.7±2.9*		
3 mo						
6 mo	-12.0 (-13.8 to -10.2)			-5.8±5.3*		88.7±10.5
12 mo		-4.7 (CI: -6.3 to -3.1 kg)		-3.9±6.0*	-14.5±1.7	91.8±11.3
24 mo			-5.5±7.0*			
Percent change (%)	-12.9% (CI, 4.8% to 10.9%	-5.5	-6.0	-3.9	-15.4	-5.6

All calculated values are presented as figures with one decimal number.

Table III. Results - BMI.

BMI kg/m2	Foster (2010)	Wycherley	Lim	Morgan	Tay	Brehm	Foster (2003)
Baseline	36.1 (3.59)	33.5 ±0.8	32.3 ±3.1	31.9 ±2.2	33.9 ±4.3	33.17±1.83	33.9±3.8
2 mo							
3 mo							
6 mo							
12 mo		-5.3 ±0.8					
24 mo							
Percent change (%)		-15.8					

Table III. Continued.

BMI kg/m2	Yancy	Gardner	Shai	Dansinger	Brinkworth	McAuley
Baseline	34.6±5.2	32±4	30.8±3.5	35±3.5	33.6±0.7	
2 mo		-1.60±0.98		-4.7±2.9		
3 mo						
6 mo		-2.16±2.14		-5.8±5.3	28.9±0.5	
12 mo		-1.65±2.54		-3.9±6.0	28.4±0.6	
24 mo						
Percent change (%)		-5.2		-11.1	-15.5	

Table IV. Results - Cardiovascular Risk Factors.

	Foster (2010)	Wycherley	Lim[1]	Morgan	Tay	Brehm	Foster (2003)[2]
Triglycerides (mmol/L)							
Baseline	1.28±0.62	1.70±0.14	1.8±1	1.65±0.70	1.60±0.69	1.68±0.15	1.48±1.28
2 mo				1.08±0.44			
3 mo	0.83		1.1±0.6			1.04±0.10	-22.0±26.6
6 mo	0.83			1.01±0.33	0.96±0.35	1.29±0.17	-20.6±32.8
12 mo	0.92	1.13±0.13	1.6±0.7				-28.1±23.6
24 mo	1.14						
HDL (mmol/L)							
Baseline	1.20±0.35	1.41±0.05	1.3±0.3	1.22±0.23	1.42±0.28	1.34±0.07	1.21±0.3
2 mo				1.24±9.25			
3 mo	1.25		1.4±0.2			1.40±0.07	11.4±20.3
6 mo	1.36			1.14±0.32	1.67±0.36	1.52±0.07	3.6±14.8
12 mo	1.40	1.69±0.10	1.4±0.3				0.5±21.2
24 mo	1.40						
LDL (mmol/L)							
Baseline	3.11±0.67	3.22±0.16	3.1±1.7	3.72±0.52	3.24±0.93	3.23±0.14	3.35±0.78
2 mo				3.59±0.73			
3 mo	3.29		3.4±1.0			2.92±0.14	6.2±20.4
6 mo	3.12			3.56±0.76	3.19±0.94	3.21±0.15	3.6±14.8
12 mo	2.89	3.82±0.25	2.8±0.7				0.5±21.2
24 mo	2.98						
Tot-C (mmol/L)							
Baseline	4.88±0.78	5.40±0.16	5.9±1		5.3±0.93	5.34±0.16	5.18±0.87
2 mo							
3 mo			6.0±1.1			4.80±0.15	2.0±16.3
6 mo					5.37±1.19	5.31±0.18	3.3±10.9
12 mo		6.00±0.27	5.5±0.8				0.2±12.7
24 mo							
Syst-BT (mmHg)							
Baseline	124.3±14.1	134±3	129.8±15.1	135.0±15.1	133.1±14.4	116±3.23	120.5±11.0
2 mo							
3 mo	116.6		119.3±12.7			112±2.36	-3.1±12.1
6 mo	116.9				120.8±11.5	114±2.82	-3.2±12.7
12 mo	121.1		119.2±10.6				-1.6±12.2
24 mo	121.6						
Diast- BT (mmHg)							
Baseline	73.9±9.4	73±3	77.2±13	83.0±10.7	73.6±11.6	79±2.69	74.6±8.5
2 mo							
3 mo	68.4		73.4±9.5			72±2.06	-3.5±14.5
6 mo	68.8				69.0±11.7	74±2.23	-5.5±14.7
12 mo	70.7		70.6±12.1				-6.1±15.6
24 mo	70.7						

	Foster (2010)	Wycherley	Lim[1]	Morgan	Tay	Brehm	Foster (2003)[2]
Fasting glucose (mmol/L)							
Baseline		5.55±0.09	5.4±0.6	5.59±0.45	5.67±0.57	5.51±0.14	
2 mo				5.52±0.43			
3 mo			5.3±03			5.21±0.15	
6 mo				5.30±0.61	5.49±0.48	5.01±0.12	
12 mo		5.33±009	5.5±0.3				
24 mo							
Fasting Insulin			mU/L	pmol/l	mU/L	µIU/ml	
Baseline			10.9±5.8	73.2±35.1	9.15±4.82	16.9±1.8	
2 mo				75.2±83.6			
3 mo			7.0±3.7			11.6±1.2	
6 mo				54.8±32.4	6.17±3.48	14.4±1.4	
12 mo			9.4±4.4				
24 mo							

Table IV. Continued.

	Yancy	Gardner	Shai	Dansinger	Brinkworth	McAuley
Triglycerides (mmol/L)						
Baseline	1.78	1.41±0.88	2.05±1.32	1.71±1.11	1.67±0.13	1.87±0.82
2 mo		0,82±0.75		1.24±0.81		
3 mo						
6 mo	0.94	1.01±0.73	1.60	1.50±0.60	0.95±0.06	1.04±0.40
12 mo		1.08±0.67		1.69±1.32	1.09±0.11	1.40±0.93
24 mo			1.78			
HDL (mmol/lL)						
Baseline	1.43	1.37±0.36	0.97±0.22	1.24±0.41	1.45±0.05	1.14±0.29
2 mo		1.36±0.20		1.35±0.17		
3 mo						
6 mo	1.57	1.50±0.25	1.09	1.42±0.19	1.68±0.07	1.28±0.35
12 mo		1.50±0.24		1.40±0.23	1.75±0.09	1.26±0.38
24 mo			1.19			
LDL (mmol/L)						
Baseline	4.07	2.82±0.75	3.03±0.89	3.52±0.80	3.2±0.1	3.8±0.9
2 mo		2.88±0.61		3.56±0.52		
3 mo						
6 mo	4.11	2.86±0.58	3.06	3.39±0.47	3.3±0.2	3.8±1.0
12 mo		2.84±0.58		3.17±0.83	3.8±0.2	3.7±1.0
24 mo			2.95			
Tot-C (mmol/L)						
Baseline	6.32			5.53±0.80	5.4±0.2	5.8±1.1
2 mo				5.47±0.70		
3 mo						
6 mo	6.11			5.49±0.62	5.4±0.2	5.2±1.2
12 mo				5.32±0.80	6.0±0.2	5.6±1.3
24 mo						

	Yancy	Gardner	Shai	Dansinger	Brinkworth	McAuley
Syst- BT (mmHg)						
Baseline	X	118±11	130.8±15.1	129±17	132.7±2.3	131±14
2 mo		-6.8±8		123.6±15		
3 mo						
6 mo	-9.6	-6.4±9.5		122.3±12	118.5±1.7	126±15
12 mo		-7.6±11.0		129.3±17	118.9±2.0	126±15
24 mo			-126.9±12.8			
Diast-BT (mmHg)						
Baseline	X	75±8	79.4±9.1	77±9	72.3±1.8	84±10
2 mo		-2.9±6.2		71.5±9.0*		
3 mo						
6 mo	-6.0	-3.3±6.9		69.7±7.4*	66.3±1.7	81±8
12 mo		-4.4±8.4		74.4±10.3*	66.0±2.0	80±9
24 mo			78.6±8.7			
Fasting glucose (mmol/L)						
Baseline		5.11±0.50	5.14±1.58	7.06±3.44	5.7±0.1	5.1±0.6
2 mo		5.09±0.38		7.00±1.89		
3 mo						
6 mo		5.12±0.42		6.27±1.89	5.5±0.1	4.8±0.6
12 mo		5.01±0.74		7.2±2.33	5.4±0.1	4.9±0.7
24 mo						
Fasting Insulin		µU/mL	µU/mL	µlU/mL	mU/L	
Baseline		10±7	14.1±10.2	22±16	7.9±0.6	
2 mo		7±3.9		-6.5±15		
3 mo						
6 mo		7.2±4		-4.1±15	4.8±0.3	
12 mo		8.2±4.8		-2.3±9	4.8±0.5	
24 mo						

1) Data from Baseline, 3 months and 15 months (not 12 months).

2) Except for baseline values, values for 3, 6 and 12 months are percentage change from baseline value.

Foster 2003: Data from completers only.
Tay: Data from completers only.
Bhrem: Data from completers only.
Yancy: Data from completers only.
Dansinger: Data is from cmpleters. At Baseline n= 40, at 2 mo n=31, at 6 mo n=22, at 12 mo n=21
Brinkworth: Data from completers only.
McAuley: Data from completers only.
Gardner: Intention to treat - where Baseline values were carried forward for missing values

Table V: Results - Cardiovascular risk factors, per cent change from baseline.

(%)	Foster 2010	Wycherley	Lim*	Morgan	Tay	Brehm	Foster 2003
Triglycerides							
6 mo				-38.8	-40.0	-23.2	
12 mo		-33.5	-11.1				-28.1±23.6
24 mo	-10.9						
HDL							
6 mo				-6.6	+17.6	+13.4	
12 mo		+19.9	+7.7				+18.2±22.4
24 mo	+16.7						
LDL							
6 mo				-4.3	-1.5	-0.6	
12 mo		+18.6	-9.7				+0.5±21.1
24 mo	-4.2						
Tot-C							
6 mo					+1.3	-0.6	
12 mo		+11.1	-6.8				+0.2±12.7
24 mo							
Syst-BT							
6 mo					-9.2	-1.7	
12 mo			-8.2				-1.6±12.2
24 mo	-2.2						
Diast- BT							
6 mo					-6.3	-6.3	
12 mo			-8.6				-6.1±15.6
24 mo	-4.3						
Fasting glucose							
6 mo				-5.2	-3.2	-9.1	
12 mo		+3.9	-1.9				
24 mo							
Fasting Insulin							
6 mo				-25.1	-32.6	-14.8	
12 mo			-13.9				
24 mo							

Table V. Continued.

	Yancy	Gardner	Shai	Dansinger	Brinkworth	McAuley
Triglycerides						
6 mo	-47.2					
12 mo		-32.4		-1.3	-34.7	-25.1
24 mo			-13.0			
HDL						
6 mo	+9.8					
12 mo		+9.3		+13.3	+20.7	+10.5
24 mo			+22.4			
LDL						
6 mo	+1.0					
12 mo		+0.7		-9.9	+18.8	-2.6
24 mo			-2.6			
Tot-C						
6 mo						
12 mo	-3.3			-3.8	+13.0	-3.5
24 mo						
Syst- BT						
6 mo	X					
12 mo		-6.4		+0.2	-10.4	-3.8
24 mo			-3.0			
Diast-BT						
6 mo	X					
12 mo		-5.9		-3.4	-8.7	-4.8
24 mo			-1.0			
Fasting glucose						
6 mo						
12 mo		-2.0	*	+2.0	-5.3	-3.9
24 mo						
Fasting Insulin						
6 mo						
12 mo			**	-10.5	-43.0	-39.3
24 mo		-18.0				

All calculated values are presented as figures with one decimal number.

X = missing values. Only decrease is given, but not baseline value, so no known percentage change from baseline

*Gluose:
Non-Diabetes: +1.2. Percent change: +1.40
Diabetes: +1.3. Percent change: +1.40

**Insulin:
Non-Diabetes: -3.7. Percent change: -26.2 %
Diabates: -2.2. Percent change: -11.9 %

Results

Weight loss

All studies reported statistically significant weight loss after the completion of the LC dietary intervention, ranging from a weight loss of approx. 3.3% to 15.8% from baseline value.

Some studies reported that the difference in weight loss shown in the LC group, when compared to the other dietary intervention group(s)/control group(s) at the time of completion, was not statistically significant. This was true for the following studies: Foster 2010, Foster 2003, Wycherley, Morgan, Tay, Dansinger, Brinkworth.

Others reported differences in weight reduction, where the mean weight loss for subjects in the LC group in comparison to the other dietary intervention group(s) was statistically significant. This was true for Brehm, Yancy, Gardner, Shai (the latter, where both the LC group and the Mediterranean group differed from the other two groups) and McAuley (the HF and HP had statistically greater weight loss when compared to the HC group).

Most of the analyses and data collection in the studies are secondary analyses, where subjects who did not complete the study were excluded from the final analysis. Brehm also reported that the weight loss achieved in the LC group was significantly greater when compared to the other LF group both when using an intention to treat (ITT) analysis approach and a secondary analysis, where only the subjects who completed the whole dietary intervention were included.

Furthermore, some studies reported differences between the LC and the alternative diet(s) at certain assessment points during the intervention.

Foster 2010, Foster 2003, Gardner and McAuley reported that the LC group had a greater weight loss when compared to the other diet groups (LF in Foster 2010 and 2003 and the ZONE, LEARN and ORNISH for Gardner and HP and HC in McAuley) at certain assessment points during the intervention. Foster 2010 and Foster 2003 report that these differences were seen at 3 and 6 months, respectively, but that the differences between dietary groups did not persist at the last assessment point at 2 years and 1 year, respectively. Likewise, Gardner reports that the weight loss for the

subjects on the LC diet at intermediate assessment points at 2 and 6 months was significantly greater when compared to the other three diets (these diets did not differ significantly from one another at any point), but at the 1 year assessment, the difference in weight loss between the LC and the other diets was not statistically significant. McAuley noted differences in weight loss between the three groups - the low-carbohydrate groups lost significantly more weight than the HC diet, but differences were also seen within the lower-carbohydrate groups: the HF lost more than HP at 2 months. At 4 months, the two groups showed similar weight loss, but at 6 months, the HP showed greater reductions than the HF group.

BMI

Very few articles reported the changes in BMI from baseline. The studies were this data is provided are Wycherley, Gardner, Dansinger and Brinkworth. The value of change in BMI ranges from -5.0 to -15.8 %.

Wycherley reports that changes in BMI in the LC group were not different from LF group. Similarly, McAuley reports that there was an appreciable reduction in BMI which were comparable in all groups.

Cardiovascular risk factors

Triglycerides (TAG)

All the studies concluded that TAG decreased at the end of the intervention.

The per cent change from baseline ranged from a decrease of approx. 1.3 % to 47.2 %. In the studies where the dietary intervention lasted 6 months, there was on average a greater decrease in TAG from baseline values than studies of longer duration. The values for the aforementioned were all between approx. -23.2% to -47.2%, while the studies that lasted 12 months, range from approx. -1.3%-34.7%. Of the two studies that conducted a dietary intervention over 2 years, the TAG values were 10.9 % for Foster 2010 and 13.0 % for Shai.

Some studies reported a significant difference in triglycerides values between the different dietary intervention groups at the end of the intervention; the LC group showed greatest decreases. This was true for Morgan, Tay, Yancy, Gardner, Shai and Brinkworth, McAuley (HF and HP had significantly greater reductions compared to the HC group).

Some studies reported that there was no difference of statistical significance between groups at the end of the intervention: Foster 2010, Whycherly, Lim, Brehm, Foster 2003

Although there was no significant difference between groups at the last assessment of the dietary intervention, some studies reported that there were statistical significant differences between dietary groups at certain assessment points during the intervention. This was true for Foster 2010, Lim and Gardner, where the reduction in TAG were greater for the LC group when compared when the other groups at certain points, but that these differences did not persist at 12 and 24 months for Foster 2003 and Foster 2010, respectively, and at 15 months for Lim.

Dansinger reported no significant change in TAG at 1 year, which was also true for the other diet groups in the study.

High-Density-Lipoprotein (HDL-C)

All studies reported an increase in HDL-C from baseline values, with the exception of Morgan where HDL decreased by approx. 6.6% at 6 months - referred to as unchanged in the article. For all the other studies, the increase in HDL from baseline ranged from approx. 7.7 % in Lim to 22.4 % in Shai.

The studies that reported that the LC diet had a greater increase in HDL in comparison to other diet groups at the end of intervention were the following: Foster 2010, Tay, Foster 2003, Yancy, Shai, Gardner, Brinkworth, and McAuley (not statistical difference between the LC and the HP, but in comparison to HF).

Some studies reported no difference of statistical significance between groups at end of the intervention: Wycherley, Lim, Brehm and Dansinger (only Ornish group did not show similar results).

Although Lim reported that there were no differences between groups of statistical significance in HDL values at the end of the intervention, there was a difference between the LC and the other diet groups at assessment point at 3 months. This could no longer be observed at th last assessment point at 15 months.

Low-Density-Lipoprotein (LDL-C)

Most studies reported a small decrease or increase ranging from approx. -9.9 % (Dansinger) to approx. +1.0 % (Yancy) in LDL. However, Wycherley and Brinkworth presented data that showed a much greater increase of approx. 18.6 % and 18.8 %, respectively. In both studies, the subjects completed a 12-month intervention.

In the following studies, the LDL-C values did not change significantly from baseline values: Foster 2010, Morgan (decreased significantly in all other groups), Tay (decreased in HCLF group), Brehm, Yancy, Gardner (no significant differences between groups at end point, but at 2 months, changes in LDL favored the other groups) and Shai.

In Lim and Dansinger there was a percentage change from baseline of approx. 9.7 % and 9.9 %, respectively, but in the latter case it was reported that this change from baseline did not reach statistical significance. In the case of Lim, there were no differences between groups in the study, whereas the other diet groups in Dansinger all had a decrease of LDL-C levels of statistical significance.

Wycherley and Brinkworth had an increase of LDL-C levels of statistical significance from baseline values, but also in comparison to the other groups in the studies which did not experience such great increases in LDL-C levels.

Blood pressure (BP)

In all studies but one, subjects had a decrease in both systolic and diastolic blood pressure. The percentage changes from baseline varied from approx. +0.2 % (Dansinger) and -10.4 %

(Brinkworth) for systolic BP. For diastolic BP the percentage change from baseline values varied from approx. -1.0% (Shai) to -8.7 % (Brinkworth).

Diastolic BP was statistically lower in the LCHF group than the HC group

Fasting plasma glucose and Insulin

Not all studies reported fasting glucose and insulin values. Of those who did, changes in fasting plasma glucose from baseline values ranged from an increase of approx. 4.0% (Wycherley) to a decrease of approx. -9.0% (Brehm.) Changes in fasting plasma insulin ranged from approx. -10.5 % to - 43.0 %.

The following studies reported that the percentage change (reduction) of fasting glucose from baseline was considered statistically significant: Brehm (no difference between groups) and Brinkworth (independent of diet and sex). Morgan reported a strong trend of decrease in fasting plasma glucose levels, but was even more favorable for the other diet groups in the study. Lim reported that there was a group by time interaction at 3 months, but that these differences in glucose levels did not persist at 15 months. Dansinger reported that no diet significantly altered plasma fasting glucose.

The following studies reported that the percentage change (reduction) of fasting insulin from baseline was considered statistically significant: Morgan (evidence of diet-gender interaction), Tay, Brehm, Shai, Gardner and Brinkworth (independent of diet and sex), McAuley. (Morgan, Tay, Brehm, Shai, Gardner and McAuley report that there was no significant difference between groups.)

Dansinger reports that the diets with lower carbohydrate contents were more likely to reduce insulin in the short term, but that the subjects on the Atkins failed to significantly reduce mean fasting insulin levels at 1 year. Similarly, Lim reported that there was a time by group interaction at 3 months, but that these changes did not persist at 15 months.

Shai divided the groups into subjects with and without diabetes and reports that of the 36 subjects with diabetes, only the subjects in the Mediterranean group had a decrease in fasting plasma glucose levels. This was additionally significantly different from the increase observed in the LF

group. There was no observed change in plasma glucose levels in subjects who didn´t suffer from diabetes. Furthermore, Shai reports a significant decrease in insulin levels, with no significant differences between groups, where one group consisted of subjects suffering from diabetes and the other with subjects who didn´t suffer from diabetes.

Discussion

The purpose of this literary review was to examine the to-date published literature concerning the LC diet and its´ effects on weight and parameters of cardiovascular disease. Additionally, the aim was trying to determine whether this approach of weight loss based on the published literature could be considered more beneficial than other approaches (conventional diet and other diets), and therefore be recommended in a clinical setting for overweight and obese patients wanting to lose weight. Furthermore, it also provided the opportunity to explore whether the literature on this topic at this point in time, serves as an adequate resource for making educated evaluations and decisions in regards to diet recommendations.

When reviewing the articles, it became apparent that the outcomes of diet on weight loss and cardiovascular risk factors in these studies were varied.

Weight loss

In all the selected studies, the subjects on the LC diet experienced a significant mean weight loss at the end of the dietary intervention, whether it lasted for 6 months, 1 or 2 years. However, when compared to the weight loss in the control group(s), the LC group often had a weight loss that was comparable to the other diet(s) in the study, and most often did not yield a weight loss that was significantly greater from that of the other diet(s) in the study (20-21, 23-24, 26, 30-31, 35). This conflicts with the promises made by Atkins (12).

There was a clear trend in some studies toward a quicker and greater weight loss at 3 months or 6 months in subjects on the LC diet, but these differences failed to persist after a longer time (20, 22, 26, 28). This is also consistent with a published review article comparing LC diet without energy restriction to LF diet with energy restriction, where some of the included studies here were used, but also others (33). Important to consider is also that the weight loss observed in subjects on the LC diet during the first few weeks is considered too great and rapid to come from simply burning fat alone, and has been thought to be a result of the loss of body water; the ketogenic phase of the diet (particularly the two first weeks) consequently depletes glycogen storages and hence results in water loss, which is observed as quick weight loss, but beyond this period of time there is general

agreement that weight loss also is a result of the burning of fat (34). Why these differences failed to persist could be due to many reasons; some acknowledged reasons are the increased weight gain among the LC subjects (26). Another reason could be lack of adherence to diet with time as observed in many of the studies. This also raises the questions of adherence to this particular kind of diet, which will be addressed later.

The weight loss in the LC diet group was often compared to the weight loss achieved with the best available pharmacotherapy (20, 26).

Although Atkins claims that one can lose more weight on the LC diet (due to the shift in macronutrient composition with low COH intake and unlimited fat and protein intake), many of the presented studies do not ultimately agree with this claim. The diets compared in the various studies had a very different macronutrient composition (LC often versus conventional LF diet), but yielded in most cases similar amount of weight loss from baseline. This raised the question whether macronutrient composition in reality had little or no influence on the amount of weight lost among LC subjects, and rather that it was the reduction in calorie intake observed in the LC diet subjects that was the cause of the weight loss (26). The other diets in the studies had often been imposed an energy restriction in addition to the limitation of a specific macronutrient, while for the most part the LC diets were conducted as an ad libitum diet (See Table I). Interestingly, subjects on the ad libitum LC diet also showed a spontaneous and probably unconscious reduction in calorie intake, and the reduction in calorie intake was significant compared to baseline values and comparable to the other diet(s) in the study (whether conventional diet and/or others), who had an energy restriction imposed on them from the outset. One of these studies was Morgan who reported a 30 % decrease in caloric intake from baseline values, and that the subjects on the LC diet was thus comparable in caloric intake to those on the other diets (Table I). Similarly, Brehm, Gardner, Dansinger (all studies in which energy restriction was not imposed) reported a significant decrease in caloric intake, and that the caloric intake was comparable to that of the other subjects in other diet groups. It has been suggested that possible detrimental effects of an LC diet containing such a high percentage of fat is mitigated by the decrease in caloric intake and the associated weight loss (25).

The observation that the LC subjects reduced their calorie intake similarly to the dieters on the other diets leads to the assumption that similar weight loss is in reality only due to reduction in energy

intake (34, 35). It is no secret that this imbalance (calorie expenditure exceeding intake) results in weight loss (34). Foster 2003 also acknowledges this; when the energy content of an energy-deficient diet is stable, the macronutrient composition of the diet does not influence weight loss.

The mechanism behind the reduced energy intake among LC diet is unknown, but plausible causes presented are in particular that the macronutrient composition in the LC diet, favoring greater intake of fat and protein, influences appetite and satiety (26, 35). Another reason presented is that subjects on the LC diet in the studies found themselves limited by the food choices of this particular diet and that over time this diet was found to be monotone (26). Reduction in calorie intake could be a combination of the two, but this observation also opens of for further research on the satiety qualities of protein and fat, while little is known about the mechanisms that are responsible for this observed reduction in calorie intake.

Cardiovascular risk factors:

With weight loss, one expects to see improvements in cardiovascular risk factors, such as increase in HDL and decrease in LDL, total-cholesterol and triglycerides (14, 23). Atkins also promises improvements in these parameters (12).

HDL and TAG

In the presented studies, a repeating pattern of increased HDL values and a decrease in TAG values among subjects on the LC diet was evident, and as mentioned these are expected findings with weight loss; it is also consistent with what others studies have reported (33, 35).

These findings are interesting in terms of possible macronutrient effects on CVD risk; different dietary groups experienced similar weight loss, but had statistically significant differences in lipid profile parameters. It is uncertain how these favorable effects translate into possible prevention of CVD, and whether these seemingly beneficial changes are outweighed by the possible deleterious effects of such a diet. Although some agree that macronutrient composition may have been the main reason for the favorable CVD risk parameter changes, others disagree and conclude that the data moreover indicates that the observed benefits are secondary to the greater weight loss produced by the diet (32).

The role of HDL in preventing or causing cardiovascular disease is still unclear. There is much evidence that increased HDL levels are inversely related to the risk of coronary disease, but it is yet to be demonstrated that the increase of HDL levels either through diet or lifestyle modifications is directly related to reduction in coronary disease risk (36). So while the presented studies overall had a favorable effect on HDL cholesterol (not always statistically significant from baseline), it is uncertain whether this in the long term actually has a favorable effect when it comes to reducing risk of CVD.

Triglycerides are the most abundant form of fat in the body and provide energy for the body, hence they are necessary for the body to function normally (19). Although the role of triglycerides in relation to CVD is yet to be fully clarified, there is a direct relationship between elevated levels and disease. Hypertriglyceridemia is the condition with excess of triglycerides, and it is strongly associated to the occurrence of coronary heart disease in some people. Today the American Heart Association (AHA) guidelines dictate treatment of hypertriglyceridemia to include changes in lifestyle, weight loss and reduction of fat intake (where saturated, trans fat and cholesterol in the diet) is also strongly recommended (19, 37). The LC diet as dictated by Atkins deviates strongly from these recommendations, and encourages liberal intake of saturated fats, but on the other hand trans-fat is strongly discouraged.

In this review, although there was a significant decrease in TAG, it also becomes clear from the presented data, that studies of longer duration (2 years), TAG levels did not show as great of a decrease as in the studies of shorter duration. Foster 2010 does not acknowledge statistical significance of TAG change at 2 years, although the HDL stayed elevated and that this increase was statistical significant. It would however take more studies of longer duration, 2 years and more, to be able to determine a trend, as there were only 3 studies conducted with a 2-year duration, namely Foster 2010 and 2003 and Shai.

This observation makes it reasonable to assume that the metabolic changes in lipid metabolism that occurs when one starts on a very restrictive LC diet, also changes when the subjects again start to consume more COH, and/or perhaps even more importantly when adherence to the diet declines. The retention rate in the studies and the data analysis (whether ITT or secondary) are also valuable observations which can make it difficult to properly understand the results, but this will also be addressed later.

The suggestion is that the LC diet has an overall more favorable effect on HDL and TAG compared to a conventional diet/other diets (20). In contrast, others have shown that a reduced-fat ad libitum diet have beneficial effects on CVD risk on subjects with glucose intolerance, including tot-cholesterol, LDL, cholesterol and blood pressure during a 5 year period, but also particularly so during the first 6 months (6). Furthermore, others report that a low fat diet with high intake of complex carbohydrate does not produce adverse effects on CVD risk, (when weight loss occurs simultaneously), and additionally decreases mortality among high risk subjects (7).

LDL

When it comes to the LDL lipid profiles, the studies presented differing data. Most studies reported small, and not statically significant changes (decrease or increase), but two studies showed a significant increase, namely Brinkworth and Wycherley. The two were both 12-month intervention studies. Most studies recognize the valid concerns that have previously been raised regarding increased LDL levels, due to the potential detrimental effects a diet high in saturated fat is expected to have on LDL levels (22). In a meta-analysis, it was shown that the LC diet had unfavourable effects on LDL levels when compared to an LF diet (33). Concern was also been expressed in regards to the lack of change, as LDL levels are expected to decrease with moderate weight loss, and the observation that the LDL levels were subject to substantial individual variability (24, 26, 32).

In Foster 2010, it is described that although LDL increased at 3 and 6 months, but not reaching statistical significance, the differences in LDL levels between the two groups (decrease in LF group) was statistically different. Similarly, Foster 2003 also noted a trend of increasing LDL levels in the LC group, whereas it was decreased in the LF group. Again although the changes in themselves were not statistically significant, the difference between groups was great enough to satisfy statistical significance.

In Tay, overall LDL levels did not change. However, observations were made that 36% of subjects on the LC diet experienced an increase of at least 5 %, compared to 12% on the LF diet. Additionally, 24 % of the subjects experienced an LDL increase greater than 10%, compared to 10% in LF diet. 58% of the subjects on LC diet experienced a decrease in LDL levels, compared to 79% on the LF diet. Furthermore, effect of gender was observed, where LDL levels became more

unfavorable in men than women on the LC diet. No such gender effect was observed on the LF diet. In summary, Tay writes that there were great differences in individual response, where LDL levels varied substantially (one half showed a decrease, and one half showed an increase), which is believed to limit the generalizability of this diet.

McAuley observed similar results; LDL cholesterol increased by > 10 % in 8 subjects (25 %), compared to 13 % in HP and 3 % in HC group. Furthermore, although the LC diet did not markedly increase LDL, LDL levels here were significantly higher than the LDL levels observed in the HP group - interestingly, the two groups had similar weight losses.

Morgan observed that the decrease in TAG was associated with the predominance of small, dense LDL, which are associated with lesser risk of CVD and less atherogenicity. The other studies do not comment on LDL particle size and the possible favorable alterations in LDL particle size.

Much research has been done on LDL and the atherogenicity of the difference species of LDL. Traditionally, one divides LDL into two subclasses: large LDL, which are rich in cholesterol, and small, dense LDL, which contain less cholesterol (38). It has also been suggested to divide LDL into three classes to improve accuracy: Very large LDL (LDL I), large LDL (LDL II) and small LDL (LDL III) (38). Research has shown that the lipoprotein associated with the highest atherogenicity are the small dense LDL particles, and that individuals where this subclass of LDL is the most predominant one, are more at risk of CVD (39). Furthermore, individuals with a lower than average number of LDL particles, and additionally where LDL subclass II is predominant, have in comparison a lower risk of CVD (38). Berneis describes an atherogenic lipoprotein phenotype: abundance of small dense LDL particles, together with other features, including increased levels of TAG rich in lipoprotein remnants and IDLs, decreased levels of HDL and insulin resistance. All these factors contribute to an overall increased risk for coronary heart disease, where this abundance in small LDLs in related to a 3-fold increase in coronary heart disease compared to individuals who have a predominance of larger LDLs (39).

In summary, while the LC diet had favorable effects on the HDL and TAG, which has been acknowledged as being possibly due to the macronutrient composition of this diet, the effects on LDL levels seem to be more uncertain. Some suggest that the LC and LF diet produce different effects on LDL and TAG that are dependent on the initial type of LDL/LDL phenotype (23). Based

on this, there is a suggestion that the potential favorable changes in TAG and HDL are possibly outweighed, or should at least be weighed against, the potential unfavorable changes in LDL values when deciding whether an LC diet is a viable option for an overweight person who wants to lose weight (33). This is supported by the general concern expressed in some studies that point out that there seems to be an individual response to the LC diet on LDL-levels (24, 32), which to date is impossible to predict. This individual variability makes it difficult to make recommendations in regards to use of the LC diet to a general population. It is suggested that this diet might be good for overweight subjects who additionally suffer from diabetes type II and subjects who have known hypertriglyceridemia (17). However, because the individual variability is so great, it seems that in order to be able to make adequate evaluations, more research is required to find out whether certain genetic dispositions are responsible for the altered lipid metabolism which produce an increase in LDL levels, and if so, how to separate these individuals from others embarking on the LC diet. More research should also be conducted to learn more about the composition of the LDL particles, and possible alterations from small dense, to large, less atherogenic LDL particles suggested to be the case in LC diet.

Insulin

Atkins bases much of the rationale behind the benefits of an LC diet on the fact that the normal western diet today results in hyperinsulinism, the main reason why people become overweight and obese. Hyperinsulinism is a state where the body produces too much insulin. It is due to cells having been desensitized to insulin (insulin resistance) because of the consumption of a diet containing a high proportion of carbohydrates, particularly refined carbohydrates. These are quickly absorbed in the stomach and require great amounts of insulin for transport, in contrast to protein and fat that require little or none at all, thus resulting in insulin resistance and increased production and release of insulin as a means of compensation. When the transport of glucose into cells still fails, the liver converts it into fat.

To illustrate how and why hyperinsulism occurs, Atkins refers to Kaplan´s "Deadly Quartet"; the quartet is made up four conditions that occurs in subjects with high insulin levels, which are likely to occur in the same person; it consists of upper-body obesity, glucose intolerance, high triglyceride levels and hypertension. This has later been referred to as Syndrome X (12). Consuming an LC diet will according to Atkins, in contrast to the LF diet, correct this syndrome and stabilize insulin and glucose levels.

Thus being a predictor of CVD, it is from a medical point of view of grear benefit to lower insulin levels as a measure of treatment and prevention. It is therefore of great interest that people suffering from overweight and obesity consume a diet, which in addition to generating weight loss and a better lipid profile, also improve insulin levels. However, when looking at the results the reviewed studies yielded, only some studies reported a favorable change in fasting insulin from baseline. Furthermore, for the most part, the changes in fasting insulin were not statistically different between groups; in other words, the LC diet was not found to be more favorable than the LF and/or alternative diets in this regard. Although the claims from Atkins are that an LC diet more effectively lowers the insulin levels, this too, is not consistent with the reported data from the selected studies. There was however a trend of decreasing glucose levels among the subjects who suffered from diabetes, and perhaps this group of patients may benefit from an LC approach. However, the data presented seems to be insufficient to make general recommendations for any group of patients and such recommendations for selective groups should therefore still be approached with caution.

Dietary Adherence and Attrition

When it comes to dietary adherence, the studies had different ways of assuring that subjects followed their assigned diets. Most studies had the participants attend the clinic every week or every two weeks for counselling or group meetings with a dietician. This would last over a period of time, often 8 weeks, and thereafter meetings would become more infrequent. Macronutrient composition data was mostly collected using 3-day food records, where participants were randomly selected. All the studies were conducted on free living people, and the food was not provided. Guides in form of pictures, recipes and the Atkins book were often provided. Only some reported good compliance to diet (21, 31).

Only the following studies provided an overview in form of a table, where the total energy consumed, as well as the distribution of macronutrients at the different stages of the intervention was presented: Lim, Morgan, Brehm, Gardner, Shai, Dansinger, Brinkworth and McAuley.

Although it is apparent from the tables that the subjects on the LC diet had a significantly lower COH intake (some more than others) when compared to the conventional diet and other diet groups,

some also showed remarkably high COH intake. Shai reported a COH intake of around 40 % at 24 months. Likewise, Lim reported a COH intake of around 36 % at 15 months. Brinkworth seems to be the study where the intake of COH was kept at the lowest levels with only close to 9 % at 1 year. In other words, although references to the Atkins diet and/or a thorough description of an LC diet and data collection were made in the studies, and seemed to be what the subjects in reality would actually follow at the outset (and thus included in this literary review), it is clear that dietary adherence was quite varied and that over time it can possibly also be characterized as questionable. Others report similar difficulties concerning adherence and that if the dietary targets had been met, it would have produced different results (35). Consequently, in retrospect, one could argue that an additional exclusion criterion should have been made based on the provided tables of the actual macronutrient consumption. The consideration was made at the outset, but was rejected because of the lack of such data in other studies. One could choose to exclude studies such as Shai and Lim based on the information on actual macronutrient composition, but because some studies did not provide this type of information, it would be wrong to exclude them. However, due to the great differences in macronutrient composition, even though supposedly the same diet, one can raise the question of the validity of comparing the data provided; this is therefore considered to be a great weakness of the individual studies, but also here, while it limits the generalizability of the conclusions and assumptions that have been made on the said data.

Another interesting aspect of the studies is also the very varied attrition rate. While Lim and Foster 2010 reported an attrition rate of approx. 57 % (17/30, but 27/30 were included in the analysis) at 15 months and 42 % at 2 years, respectively, Gardner had an attrition rate close to 12 % at 12 months. Generally, because the studies also vary in duration, it is difficult to say whether the attrition rates would compare if the duration were the same, and there is no trend other than that attrition rate is generally high. McAuley and Gardner reported the lowest attrition rates.

Some of the studies draw attention to the fact that the LC diet is a hard diet to follow in the long run, because the food choice can seem monotone and uninspiring. Another aspect is that when dietary plans are set in motion on free living people it is difficult to really control what the subjects consume. Dietary journals are prone to flaws while subjects might be subjected to the omission and/ or addition in an attempt to please the researcher. This opens up for lack of adherence to the diet (although this might not come across), and thus perhaps also lack of results. Lack of results in form

of weight loss, as a consequence to poor dietary adherence, might have contributed to lack of motivation among some subjects and consequently resulted in high dropout rates.

Further research

While it is difficult to draw conclusions that can be applicable to the general population in regards to the CVD risk factors that have been addressed earlier, an increasing focus in research is how the LC diet affects vascular function.

The concern is that the increased fat intake may have detrimental effects on endothelial function (21, 40). The parameter often explored is the brachial artery flow-mediated dilatation (FMD), which has been found to be impaired in subjects suffering from obesity, and found to be a predictor of cardiac events (41-44). Furthermore, pulse wave velocity (PWV), and augmentation index (AxI), which are indicators of arterial stiffness, are assessed. A fast PWV is associated to a stiff aorta. AI_x is an indicator of systemic arterial stiffness (21). The velocity and amplitude of the reflected pulse waves from the periphery increases with increased stiffening of the arterial tree; this results in larger waves returning to the aorta at a faster rate, thus increasing the workload of the left ventricle and well as challenging the oxygen demand (40).

One study found that weight loss resulted in reduction in PWV and other endothelial factors, but also concluded that an LC diet impaired FMD (21).

Although there has been no studies to date that have assessed the long-term effects of the LC/Atkins diet on endothelial function, there has been conducted shorter studies to assess the immediate response in FMD after meals containing a high saturated fat intake. These have shown that after such a meal, FMD is impaired (21). Likewise, FMD was reduced in a 6 week study in the LC group, in contrast to a significant improvement in the LF (AHA-modelled diet) group (41). Furthermore, because other CVD risk factors such as BP and weight were favorably and similarly improved, Phillips suggested that the changes in endothelial function were macronutrient dependent.

In another study, after 12 weeks of adaptation to a diet very low in carbohydrate, FMD was not impaired, but improved. Attention was drawn to the possible role of subjects' prior diet history and adaptation to an LC diet (45). An 8 weeks study found that when comparing an LC diet with that of an isocaloric high-carbohydrate, low-saturated fat diet, neither significantly changed FMD (46). Similarly, a 12 week study showed that FMD did not improve after short-term weight loss or long-term weight maintenance on a LC diet (47).

Another study found that when comparing a LC diet group (20 % COH) with a low-fat diet group, the latter produced a significant reduction in AI_x, whereas there was a non-significant increase in the LC group (40).

These conflicting findings pose interesting questions that are worth looking into in order to obtain a more satisfying picture of how the LC diet also possibly affect other parameters which are known predictors for CVD.

Conclusion

As stated, the aims of this literary review were to gather the available data, summarizing it and trying to draw conclusions in regards to the effectiveness of the LC diet on weight loss and possible effects on CVD risk factors. As many of the studies also conclude, it is clear that although the LC diet does seem to have some favorable effects, especially on HDL and TAG levels when compared to a conventional diet, there are other aspects which might outweigh these benefits. The individual variability in LDL levels as a response to the LC diet, remains a concern. Additionally, it is important to acknowledge that none of these studies were conducted on people with a history of CVD and that hard-end points (such as myocardial infarction, and/or death) were never tested; the LC diet however, as prescribed by Atkins, is said to be applicable on a general population suffering from overweight, regardless of CVD and CVD pathological parameters. This generalizability is repeatedly cautioned against in the reviewed studies. Furthermore, it seems to be difficult to perform a dietary intervention study on a large sample size over longer time; the poor adherence in some studies make comparisons between studies, and general conclusions which can be applied to larger populations questionable.

In conclusion, the effectiveness of the LC diet on weight loss is often similar to that of an LF diet. The effects on CVD risk factors remain unclear; this is also agreeable with what others have concluded in the past, namely that there seems to be inadequate data to be able to either make recommendations for or against such a diet (11, 33). Further research to establish the relationship between the LC diet and CVD risk factors is warranted, particularly studies of longer duration, with greater sample sizes combined with lower attrition rates and better dietary compliance.

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