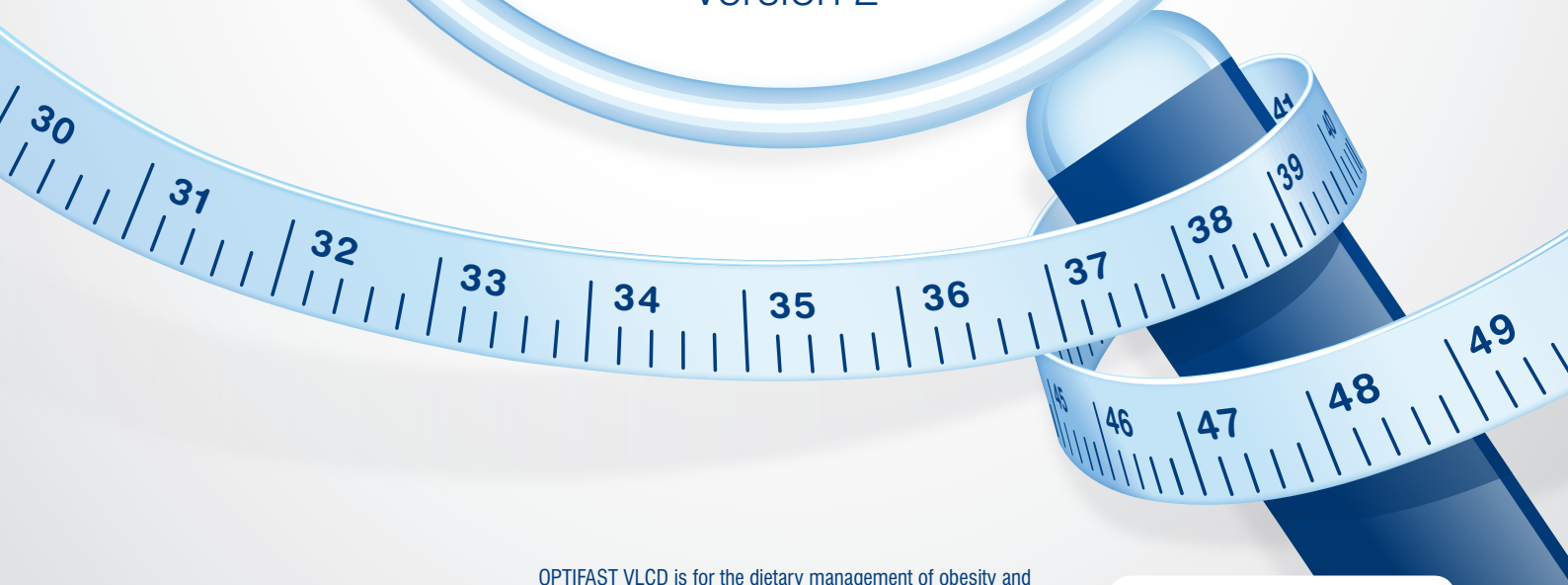
OPTIFAST® VERY LOW CALORIE DIET

Management of Complex Cases

Managing obesity with the OPTIFAST VLCD Program for people with complex cases

Version 2



OPTIFAST VLCD is for the dietary management of obesity and must be used under the supervision of a healthcare professional.
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Treatment Guidelines

The OPTIFAST VLCD Program aims to assist the healthcare professional manage patients at medical risk due to excess body fat. Overweight or obesity can be accompanied by co-morbid conditions that put the patient at extra risk and add an extra dimension to the treatment program for healthcare professionals.

While there is a comprehensive protocol for the dietary management of OPTIFAST VLCD it does not address the use of OPTIFAST VLCD in the dietary management of obesity in complex cases, such as with certain co-morbidities. With this in mind, treatment guidelines specific to the issue have been developed in order to address any uncertainty that may be experienced by healthcare professionals and assist them in the management of obesity and co-morbid conditions.

The guidelines have been developed with input from a group of healthcare professionals with expertise in the field, taking into account direct patient experience and relevant available research. For a group of important co-morbid conditions, the guidelines provide a brief review of clinical evidence, along with recommendations on patient suitability, adaptations to the program, and contraindications and precautions.

These guidelines are designed to be used alongside the existing *Clinical Treatment Protocol* and *Preoperative Protocol* for OPTIFAST VLCD. These documents are designed to support professional standards and best practice methodologies for the healthcare professionals using them.

Chronic disease management, which depends on modification of lifestyle, requires a multidisciplinary approach best delivered by a team of healthcare professionals.

Continuity of care is important, particularly where co-morbid conditions exist. Contacting other healthcare professionals who are treating a specific individual can help all involved to work together as a co-ordinated team. At all times the patient should be under the supervision of a qualified medical practitioner.

We would like to thank the following experts for their contribution, feedback and review:

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Please note:

We would appreciate any feedback or comments you may have on how to further improve the treatment guidelines and make them more relevant to you and your practice.

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Heart Failure and Ischemic Heart Disease

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Review of Clinical Evidence

- There are no studies using OPTIFAST in congestive cardiac failure (CCF) or ischemic heart disease (IHD). However, there is substantial literature on the relationship of obesity and cardiac function.
- Surprisingly, it appears that mild degrees of overweight are actually beneficial to survival in patients with heart failure. This has been referred to as "The Obesity Paradox", and has been extensively discussed in the literature.[1]
- Overall while there may been evidence that a degree of overweight or obesity is protective, the balance of data would still support the need for weight loss given the extensive data that obesity damages the heart.[2-7] In a large community-based sample, Kenchaiah and colleagues found that obesity was associated with a doubling of the risk of heart failure.[8] There is also data to show that weight loss improves cardiac function in severely obese subjects.[9-11]
- In patients at risk of arrhythmias it is important to note that studies have found no change in QT intervals during VLED treatment of up to 3 months.[12,13] One Japanese study showed that QT intervals were more likely to be prolonged in obesity per se whereas weight reduction using VLEDs actually reduced the QT interval.[14]
- There is no available literature on outcomes in patients with ongoing angina. It is possible that the rapid initial weight loss seen with Intensive Level VLED may reduce angina as left ventricular function improves.

Recommendations for Management

a) Patient Suitability

Based on the above, it is recommended that a very low energy diet (VLED) regime should be considered for patients with heart failure who are moderately or severely obese.

b) Adaptations to OPTIFAST VLCD Program

Treatment of obesity in patients with CCF and/or IHD may be complicated because of the risk of dehydration, postural hypotension and diet-induced hypokalemia. While OPTIFAST may be used in this setting, precautions need to be taken, especially during the Intensive Level.

Patients on diuretics may need the dose reduced or the diuretic ceased altogether as postural hypotension can occur. OPTIFAST contains less salt than most western diets and as it is a low carbohydrate load, a diuresis effect is likely to occur. Patients should be monitored closely, preferably under specialist care.

Many patients with CCF are on fluid restrictions and the recommendation to include 2 litres of low energy fluid a day as part of the intensive program may need to be modified to suit individual requirements. Again care needs to be taken to monitor electrolytes more frequently (twice per week during the Intensive Level).

If there are electrolyte disturbances, the intensity of the program can be reduced to a two meal a day replacement. On this regime patients usually maintain electrolyte balance even if on diuretics.

c) Contraindications and Precautions

Physicians should be wary of introducing the Intensive Level of the OPTIFAST VLCD Program to patients with unstable rhythm disorders or with unstable angina.

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Renal Disease

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Review of Clinical Evidence

- Obesity is an independent risk factor for the development and progression of chronic kidney disease (CKD). There is a secondary form of focal glomerulosclerosis, called obesity-related glomerulopathy (ORG). ORG is a characteristic feature of glomerulomegaly and is related to obesity. Improved renal function in both CKD and ORG has been demonstrated with weight reduction using hypocaloric (500kcal deficit) diets, pharmacotherapy or surgery. The best results have been obtained following bariatric surgery likely because of the greater and more sustained weight loss than non-surgical treatments.[1,2]
- There is limited data on the use of very low energy diets (VLED) in people with renal disease predicated on the belief that the increased protein catabolic load, diuresis and potential disruption to the electrolyte balance from a VLED may have an adverse effect on renal function.[3] However, when patients with T2DM, nephropathy and mean creatinine clearance 40ml/min/1.73m^2 were placed on a hypocaloric diet (740–970kcal and 62–64g protein/day) in which one or two meals were replaced by a liquid formula meal there was a reduction in proteinuria and serum creatinine with no significant change in creatinine clearance.[4] In a more recent study[5] six obese patients with advanced diabetic nephropathy (estimated glomerular filtration rate (eGFR) <40ml/min/1.73m^2) underwent a 12 week VLED (800kcal and ≥75g protein/day). There was 12% weight loss, improved glomerular filtration, with reduction in creatinine and cystatin c, and improved insulin sensitivity and glycaemia. In an Australian study OPTIFAST VLCD was prescribed as a modified low calorie diet to five patients on haemodialysis needing to reduce their weight prior to renal transplantation.[6] These patients received 3 OPTIFAST VLCD meal replacements, 1 main meal and 2 low potassium fruits per day (950kcal and 100g protein/day) and followed the diet for a median time of 364 days. There were no adverse events and all patients lost weight (median weight loss 7%, range 5.2–11%).
- It is recommended that patients with CKD should follow a diet of 0.75–1.0g protein/kg ideal body weight (IBW)/day.[7] The OPTIFAST VLCD Program satisfies this criterion for most people apart from patients on dialysis whose protein requirements are higher, 1.2–1.4g/kg/day. These patients may benefit from replacing standard OPTIFAST VLCD products with OPTIFAST VLCD ProteinPlus or use a protein supplement such as BENEPROTEIN.
- While there is limited clinical data on the use of VLEDs in people with renal disease, they have been shown to be effective in reducing weight and improving renal function without any reported adverse effects in these patients. However, such patients should be closely monitored to ensure that there is no disruption to electrolyte or fluid balance. Particular care needs to be taken in patients on a fluid restriction and such patients should be monitored by a physician while on a VLED.

Recommendations for Management

a) Patient Suitability

Before commencement on the OPTIFAST VLCD Program, electrolytes, creatinine and eGFR should be performed. The following criteria should be used to assess suitability:

Stage 1
Kidney damage but normal GFR >90mL/min/1.73m^2
May follow standard OPTIFAST program.

Stage 2
Mild insufficiency (GFR 60–89/min/1.73m^2)
May follow standard OPTIFAST program.

Stage 3
Moderate insufficiency (GFR <60mL/min/1.73m^2)
Need close monitoring with at least weekly measurement of renal function and electrolytes initially.

Stage 4
Severe insufficiency (GFR <30mL/min/1.73m^2)
Such patients should be under the care of a nephrologist who should be contacted to determine whether they are suitable for OPTIFAST VLCD. If on OPTIFAST VLCD electrolytes, renal function, calcium, phosphate and fluid balance need to be monitored regularly.

Stage 5
Renal failure (GFR <15mL/min/1.73m^2)
Their nephrologist needs to be contacted to determine whether they are suitable to follow a VLED and if so the renal team, including a specialist dietitian, needs to be closely involved in their care, as such patients usually have complex medical problems. While on OPTIFAST VLCD, electrolytes, renal function, calcium, phosphate and fluid balance need to be monitored regularly. However, those patients who are on dialysis are generally easier to manage as their electrolytes and fluid balance can be controlled with dialysis.

b) Adaptations to OPTIFAST VLCD Program

The importance of maintaining high fluid intake should also be emphasised, except for those patients on a fluid restriction or diuretic. Patients who are on a fluid restriction and/or diuretic need to be closely monitored with assessment of electrolytes and creatinine at least weekly initially and consideration should be given to consuming bars rather than shakes.

c) Contraindications and Precautions

Patients with acute renal disease are not suitable for the OPTIFAST VLCD Program, as they may need decreased or increased intakes of potassium, sodium and fluids. OPTIFAST VLCD is also contraindicated for patients in a catabolic state.

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Serving suggestion

Pharmacological Interactions

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Review of Clinical Evidence

- The use of a very low energy diet (VLED) such as OPTIFAST VLCD may influence the dosage requirements of some medications. This is important for medications that have a narrow effective therapeutic range. The mechanisms that may alter requirements include:
  1. A major change in nature of dietary intake – macronutrient and micronutrient
  2. Significant negative energy balance and resultant rapid weight loss
  3. Ketosis associated with fat catabolism
  4. Alterations in body composition with weight loss:
     a. Reduced fat/lipid compartment
     b. Altered lean body mass
     c. Altered hydration.
- Individuals receiving medication for Type 1 & Type 2 diabetes, hypertension, dyslipidaemia may need a reduction in dose or withdrawal from their medication whilst undergoing a VLED program. Such individuals should be monitored carefully in the first few weeks of using a VLED. Please refer to the appropriate section of these guidelines for the management of medications for these particular medical conditions.

Recommendations for Management

Warfarin

Changes in dietary intake of vitamin K can alter the dose of warfarin required to maintain therapeutic International Normalised Ratio (INR) levels.[1,2]

In an Irish population, it was found that the intake of vitamin K was higher in men (84µg/day) than women (75µg/day). The main contributors to vitamin K intake were; vegetables (48%), especially green vegetables (26%) with potatoes (10%), dairy products (10%), fat spreads (10%) and meat (8%) contributing the rest.[3]

a) Patient Suitability

Most patients on warfarin are suitable for OPTIFAST therapy but precautions need to be taken as described below.

b) Adaptations to OPTIFAST VLCD Program

The OPTIFAST VLCD Program requires the patient to increase the intake of green vegetables and other dietary manipulations, therefore the INR will need to be monitored soon after commencing OPTIFAST VLCD Program. It is recommended to continue with the usual warfarin dose but the INR levels should be monitored more often and the dose adjusted accordingly.

The new novel anticoagulants have a wider therapeutic window than warfarin. However, because of their relatively new release, there are no guidelines as to the effect of VLED-induced weight loss and dosage. It would seem that the usual scrutiny of appropriate doses is nevertheless important.[4]

Digoxin

Digoxin is used to treat various heart conditions. It is bound to plasma proteins and is mainly absorbed by the small intestine. Magnesium may decrease absorption of digoxin. Calcium and vitamin D may induce hypercalcaemia, increasing the drug effect.[5]

a) Patient Suitability

Digoxin is not contraindicated with the use of OPTIFAST VLCD, however due to its narrow therapeutic index, weight loss may affect blood levels of the drug.

b) Adaptations to OPTIFAST VLCD Program

Adequate monitoring of the drug is advised. Adverse effects are related to its plasma concentration however very few occur below 0.8µg/l.[6] Possible toxicity can be detected by some of the more common side effects such as nausea, vomiting, diarrhoea, blurred vision, visual disturbances, confusion, depression, nightmares, agitation and dizziness. Steady state is reached after about five days if renal function is normal (half-life is 36 hours). Concomitant medications may affect plasma levels, but there is very little evidence that digoxin levels can be altered by changes in diet.[7]

Lithium

Lithium makes the kidneys less able to concentrate urine, so you produce more urine and need to drink more water to keep up with the extra fluid loss. If you don't drink enough to keep up with the high output you can become dehydrated and develop lithium toxicity. Patients using lithium should be advised to maintain an adequate fluid intake of 2.5 to 3 litres per day and to consume a consistent intake of sodium.[5]

Some 19% of patients on chronic lithium therapy develop nephrogenic diabetes insipidus and are at risk of dehydration.[8]

a) Patient Suitability

OPTIFAST VLCD is not contraindicated in patients on lithium therapy provided extra attention is given to adequate fluid intake and serum lithium concentrations are monitored more frequently. It is recommended to liaise with the treating psychiatrist weekly then bi-monthly. Lithium may also interfere with thyroid function; therefore, thyroid function should be checked periodically.

b) Adaptations to OPTIFAST VLCD Program

Monitor fluid balance more carefully. Determine if there is any polyuria prior to starting. Concomitant medications such as diuretics, also require more frequent monitoring.

Anticonvulsants

Whilst there is no evidence showing the use of anticonvulsants with a VLED, evidence suggests that a ketogenic diet does not alter the blood levels of most anti-epileptic medication[9]. Given OPTIFAST VLCD only induces a mild ketosis there is no reason to suggest that an anticonvulsant in conjunction with a VLED will cause any problems. Therefore anticonvulsant therapy is not a contraindication to the use of OPTIFAST VLCD.

Studies have shown that long-term anticonvulsant therapy may result in vitamin D deficiency which may be associated with hypocalcaemia and elevated parathyroid hormone.[10]

Some anticonvulsants have been shown to lead to weight loss[11] and therefore could be used in the management of obese individuals.

a) Patient Suitability

Anticonvulsant therapy is not a contraindication to the use of OPTIFAST VLCD.

b) Adaptations to OPTIFAST VLCD Program

It is important to check vitamin D, calcium and parathyroid hormone status prior to starting OPTIFAST in patients who have had long-term exposure to anticonvulsants.

Corticosteroids

Chronic use of steroids (more than 20mg daily of prednisolone or its equivalent) must be evaluated carefully because of the tendency to nitrogen waste caused by the drugs.

a) Patient Suitability

Acute short-term steroid therapy of one to two weeks' duration may not be a problem. With chronic use, if the risk/benefit ratio favours treatment, these patients may require more protein to counteract potential catabolic effects of steroid therapy.

b) Adaptations to OPTIFAST VLCD Program

It has been recommended that protein requirements may be as high as 1.5g/kg/day for patients on long-term corticosteroids.[12] It should be noted that corticosteroid therapy may make treatment with a VLED more challenging due to an increase in appetite. The increased protein recommended whilst following a VLED program may assist with appetite control.

Hyperlipidaemia

Combined hyperlipidaemia will respond markedly to VLEDs.[13,14] Therefore, it is recommended to stop or decrease medication except in familial hypercholesterolemia.

Chronic use of drugs with gastrointestinal (GI) side effects

Drugs with potent GI side effects such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) need to be evaluated. If food had a significant buffering effect, a person may require antacids, cimetidine or enteric-coated aspirin to prevent GI side effects.

Other Recommendations

Patients taking other medications may still be suitable for a VLED, however it is important for the doctor to consider the potential pharmacological interactions and assess suitability on an individual patient basis.

NB: It is important to recognise that medication dosages may need to be altered when returning to a normal healthy diet following a period using a VLED.

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Type 1 Diabetes

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Main Points

- Care needs to be taken if using OPTIFAST VLCD in patients with Type 1 Diabetes (T1DM).
- The issue of obesity in people with T1DM is important for the clinician to consider, as there is an increasing number of patients with T1DM and obesity.
- The risk of hypoglycaemia and ketosis needs to be carefully monitored. However, with appropriate insulin adjustment, there may be less hypoglycaemia while on a VLED because of the reduced likelihood of insulin to carbohydrate mismatch.
- Glycaemic control is critical to reducing the risk of diabetic complications. Reduction of insulin dose needs to be matched to the change in carbohydrate and energy intake. The established targets of glycaemia, with avoidance of hypoglycaemia, and management of other established cardiovascular risk factors should be priority issues in the management of T1DM.

Review of Clinical Evidence

- Along with the rising epidemic of obesity, the prevalence of obesity in T1DM is also increasing and evidence is emerging that obesity can trigger T1DM in susceptible individuals.[1] Obesity also exacerbates both micro and macrovascular complications in people with T1DM.[2]
- The landmark Diabetes Control and Complications Trial (DCCT) in T1DM showed an average 5.1kg vs 3.7kg increase in weight with intensive insulin therapy compared to conventional treatment.[3] An 18-year follow-up of this trial found an increase in obesity from 3.4% at baseline to 22.7% possibly due to the community rise in obesity as well as an increase in the intensification of insulin therapy (7% at baseline to 82% at follow-up).[4] Thus increasingly patients who are obese and have T1DM will be seeking assistance with weight loss.
- Reduction in body weight is associated with an increase in hypoglycaemia that may be due to a number of factors including reduced carbohydrate intake, increased insulin sensitivity and change in physical activity.
- There are no studies on the use of a VLED in people with T1DM. Two studies have been done in which people with T1DM (n=14 in each study) were fasted for a week and then placed on a low calorie diet (LCD, 5000kJ and 150g carbohydrate). With the LCD there was a reduction in fat mass, preservation of lean mass, and a reduction in insulin dose but HbA1c was unchanged. There were no adverse events with fasting (in which patients just received a basal dose of insulin and essential electrolytes and vitamins) or the LCD.[2,5] When mice with streptozitocin induced T1DM were placed on a ketogenic diet, glucose levels returned to normal despite no treatment with insulin. In another study using a mouse model of T1DM in which the mice also had nephropathy, those treated with a ketogenic diet had normalisation of glucose levels in a week and near resolution of their albuminuria by 8 weeks. All mice on the ketogenic diet survived whereas a third of those on the chow diet died within 2 weeks.[6]
- VLEDs are associated with ketosis, a metabolic response in which ketones (acetoacetate and beta-hydroxybutyrate) are produced by the liver from the breakdown of fatty acids as an alternative fuel source when glucose is in short supply. This process is primarily driven by a reduced carbohydrate intake and is likely to occur with carbohydrate intakes of 50–100g/day. The OPTIFAST VLCD Intensive Level provides approximately 60–70g/day carbohydrate. The urine ketone levels seen in subjects consuming VLEDs is around 0.5mmol/L but may be as high as 1.5mmol/L with ketogenic diets. These levels are still much lower than the levels in diabetic ketoacidosis that are usually ≥3mmol/L and often much higher.[7]
- The appetite suppressive capability of VLEDs may be improved with the genesis of mild ketosis.[7] The insulin dose can be adjusted to maintain mild ketosis with avoidance of ketoacidosis.[8] Thus the ketosis seen with a VLED should not pose any problems for subjects with T1DM.
- While there is little literature on the use of VLEDs in patients with type 1 diabetes, with appropriate medical supervision, patient education and patient selection, VLEDs can be used in patients with T1DM.

Recommendations for Management

a) Patient Suitability

An OPTIFAST VLCD Program for weight loss can be considered in selected patients with T1DM if used with close follow up from their diabetes specialist.

b) Adaptations to OPTIFAST VLCD Program

The major clinical issue for patients with T1DM is hypoglycaemia because of the severe reduction in carbohydrate intake that a VLED supplies. Therefore, it is imperative that the insulin dose be adjusted at the start of a VLED program.

Most patients with type 1 diabetes are on a basal bolus regimen of intermediate or long acting insulin once or twice a day, and short acting insulin three times per day prior to each meal; however, an increasing number of patients are using insulin pump therapy. The short acting or bolus insulin covers the carbohydrate load with each meal. OPTIFAST VLCD product provides 18.2–23.4g of carbohydrate per serve, hence it is important to reduce the short acting insulin. In patients who are aware of their carbohydrate to insulin ratio, a suitable dose adjustment should be made.

One method to estimate the carbohydrate to insulin ratio is the **'500 rule'** where 500 is divided by the total insulin daily dose.

For example, if the total insulin daily dose is 100 units, then divide 500/100=5.
The Carbohydrate:Insulin ratio is 5.
This equates to 5g carbohydrate for 1 unit of insulin.

If taking an OPTIFAST VLCD meal replacement with 20g of carbohydrate then, divide the carbohydrate content of the meal by the Carbohydrate:Insulin ratio. For example;

- 20/5=4. Therefore, the dose should be 4 units of rapid acting insulin with the OPTIFAST VLCD meal.

It is recommended to start with 1 or 2 meal replacements on initiation to work out the bolus (rapid insulin) dose before embarking on the full Intensive Level.

A reduction in the basal insulin dose is also necessary due to the expected reduction in hepatic glucose production with a VLED. At the commencement of the full Intensive Level of the OPTIFAST VLCD Program, a 50% reduction in the dose of the basal insulin is suggested as a starting point. Patients should be instructed to monitor their blood glucose levels more frequently and the results should be reviewed regularly. Further adjustment of both basal and bolus insulins should be made to prevent hypo and hyperglycaemia.

Extra care should be taken soon after the diagnosis of T1DM. Patients should be very familiar with all aspects of self-management before starting a VLED.

It is imperative that patients monitor glucose more frequently for the first few days (at least 4 times – once before each meal and before going to bed). For optimum management, it is recommended that patients start the regimen on the weekend, when they can be at home and thus more attentive to the symptoms of hypoglycaemia. If the predominant form of hypoglycaemia is a mismatch between insulin and carbohydrate intake then a VLED may actually improve the situation. If someone is experiencing severe hypoglycaemia they should be referred to their diabetes team for review of their management and further education.

Patients should be counselled to avoid at risk behaviours (e.g. driving, swimming) until they are familiar with the effect of the OPTIFAST VLCD Program on their glycaemic profile.

Mild ketosis may be present while on the Intensive Level of the OPTIFAST VLCD Program. The expected blood ketone level is 0.3–0.7mmol/L and this is likely to persist while the individual remains on the VLED. It is unlikely that there would be an increased risk of ketoacidosis, especially if the blood glucose remains acceptable and the insulin is taken regularly. It is recommended that blood ketones be monitored at least in the first week that patients are on a VLED. A finger prick ketone level >1.0mmol/L should be discussed with a diabetes professional.

It is extremely important that patients with type 1 diabetes do not have their insulin stopped, no matter how low the insulin dose is, otherwise they risk developing ketoacidosis. Healthcare professionals should also be aware of the possibility that patients may significantly reduce or withhold insulin as a weight management strategy. The risks of this practice may need to be discussed with your patient.

c) Contraindications and Precautions

Care must be taken if the patient with type 1 diabetes also has chronic renal failure.

Another potential side effect is an aggravation of postural hypotension in patients with autonomic neuropathy. There are no obvious risks in patients with retinopathy or vascular disease.

Care should be taken if the patient has a history of an eating disorder, as these patients are more likely to omit insulin.

Case Study

Tara is a recently married 26 year old woman with T1DM for 10 years, complicated by mild non-proliferative retinopathy and microalbuminuria.

She weighs 100kg, has a BMI of 40kg/m^2 and has slowly continued to gain weight at about 2kg per year since adolescence.

Her HbA1c is generally between 8 and 9% and she is on a basal bolus regimen using 88 units of insulin daily (40 units long acting and 16 units short acting with each meal). She has tried metformin but is unable to tolerate the gastrointestinal side effects.

She finds it frustrating that the pattern of meal-time insulin and BGL monitoring (at least 4 times daily) appear to not follow a particular pattern in that sometimes her glucose levels are very high but at other times she has unexplained hypoglycaemic episodes. She has seen dietitians over the past 10 years and implemented recommended dietary behaviour but her weight has not reduced. She is screened for other associated conditions including hypothyroidism and has no other medical cause for insulin resistance or weight gain.

Her diabetes specialist suggests a trial of the OPTIFAST VLCD Program whilst being closely monitored. The goal is to reduce her weight to see if it helps with controlling her average blood glucose, avoiding mismatch in dosing causing hypoglycaemia and achieving weight reduction.

She starts with replacing one meal a day with an OPTIFAST VLCD product to see how to adjust her short acting insulin dose. She has not previously determined an insulin to carbohydrate ratio, but using the 500 rule she starts with a ratio of 5.68. She tries the Berry Crunch Bar, which contains 19.5g carbohydrate and takes 3 units of short acting insulin, which is about a quarter of her usual meal time dose. She does a blood glucose check 2 hours after she has eaten the Bar to see the effect of the dose, which is higher than her recommended post prandial target. When she next has a Berry Crunch Bar she takes 4 units of her short acting insulin and has a better post prandial glucose level.

She then supplements 2 meals a day while trialling a range of the OPTIFAST VLCD products to see what she likes best. She finds that her dose is 3–4 units of rapid acting insulin with each supplement depending on the carbohydrate content. She starts to have some overnight and early morning borderline low

glucose levels and reduces her long acting insulin from 40 to 30 units. After finding that she is stable on this she decides to embark on the Intensive Level of the OPTIFAST VLCD Program, with 3 meal replacements. She reduces her long acting insulin to 20 units (half her initial dose) and continues with 4 units of short acting with each supplement. She does additional monitoring before and 2 hours after each replacement meal.

She continues this for 10 days and finds that she feels quite well on the program. Her blood glucose levels range between 4.5–10mmol/L with no hypoglycaemia. She checks her blood ketone level for interest and it is 0.6mmol/L. Routine blood tests at this time demonstrate normal renal function and no electrolyte disturbance. After 3 weeks she has lost 6kg and due to borderline hypoglycaemia reduces her insulin dose further.

She is able to continue the Intensive Level for 12 weeks by which time she has lost 20kg. Her ability to do more physical activity increases and she feels happier. Her HbA1c has dropped to 6.2% and she is now normoalbuminuric. Her doses are 20 units long acting, and 3–4 units short acting with meals. She reduces her meal replacements to 2 per day, and consumes 1 low carbohydrate meal for a further 6 weeks, reducing her weight to 72kg. She then starts a healthy, regular diet with the occasional OPTIFAST VLCD product, usually at lunch time. She is very keen to maintain her current weight and tries to exercise regularly. She usually manages to swim or walk 1 hour daily and does this after her evening meal to minimise hypoglycaemia.

Together with her diabetes specialist nurse, Tara decides that if her weight increased to 80kg she would recommence the Intensive Level of the OPTIFAST VLCD Program.

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Type 2 Diabetes

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Main Points

- Type 2 Diabetes (T2DM) is a common association with obesity. Perpetuating factors common to both of these conditions should be the focus of management in patients with T2DM. Tackling obesity will help to achieve health targets, reduce further complications and improve long-term quality of life.
- Weight loss has been shown to be directly related to improvements in glycaemia in patients with T2DM.
- Use of a VLED, such as OPTIFAST VLCD, is a well-established method of weight loss in T2DM.
- Improvement in beta cell function and glycaemia can occur in some patients early in the course of a VLED, which may be independent to weight loss, but rather related to the reduction in energy intake.
- Methods to improve glycaemia and reduce obesity should be implemented as soon as possible in the course of T2DM as it is more likely to result in preservation of beta cell function.
- Transition to less obesogenic agents is recommended by avoiding insulin or sulphonylurea therapy and adding metformin, SGLT-2 inhibitors, DPP-IV inhibitor or GLP-1 agonist therapy. With normal eating, acarbose may be of benefit.
- Agents that appear to promote satiety such as the DPP-IV inhibitors and, even more so, GLP-1 agonists may have an additional benefit of improving compliance with a VLED, or limiting intake when on a healthy regular diet.

Review of Clinical Evidence

- In Australia, while other metabolic risks such as blood pressure and total cholesterol have decreased, BMI and mean fasting glucose have increased. In 2008 the estimated prevalence of obesity in Australia was over 28%.[1] Obesity compounds the cardiovascular risk of diabetes and is a major risk factor for T2DM, accounting for about 80% of cases of T2DM, with about 86% of people with T2DM being overweight or obese.[2,3]
- In the Look AHEAD trial, a study that assessed the effect of lifestyle intervention on a number of health outcomes in 5000 middle-aged participants with T2DM and BMI >25kg/m^2, the caloric intake was restricted to approximately 1200–1500kcal/d and included the option for a meal replacement using OPTIFAST VLCD to achieve this. Patients were randomised to interventional lifestyle therapy or standard therapy for 4 years and monitored for up to 11 years. After 4 years, an 8% weight loss was associated with better measures of glycaemia and other metabolic risk factors including blood pressure and dyslipidaemia.[4]
- Another recent study (DiRECT Trial) in the UK looked at whether intensive weight management with a total diet replacement or VLED within primary care would achieve remission of type 2 diabetes. Diabetes remission was achieved in 86% of patients with a weight loss of 15% or more and in 57% of patients with a weight loss of 10% to 15%. The authors concluded that to achieve the degree of weight loss required for significant improvements and remission in those recently diagnosed with diabetes (<6 years) a total meal replacement program is superior to standard treatment for people with diabetes.[5]
    - Remission of diabetes was maintained at 2 years post intervention for 64% of those who lost ≥10kg. These participants continued to no longer require diabetes medication and reported a significant increase in quality of life.[6]
- Independent of weight loss, early initiation of a VLED can lead to significant improvements in glycaemic control.[7] Beta cell function improvements can be seen with improvement in dynamic insulin secretion, insulin production, modulation of pulsatility and improved synchrony.[8]
- In clinical practice, it is evident that a large subset of patients with T2DM, who appear to have a requirement for exogenous insulin, when exposed to inpatient care and periods of fasting for procedures or diagnostic tests, require much less insulin or manage with their endogenous insulin function alone. The concept of pancreatic beta cell rest for uncontrolled hyperglycaemia is increasingly popular and often involves the use of early insulin therapy. An additional method of islet rest can be achieved with a VLED. A study of 14 subjects with T2DM showed 60% responded to a very low calorie intake (<450kcal/d) with a sustained reduction in blood glucose levels (<10mmol/L). A positive response was predicted by a good response on day 2 of the diet, shorter duration of diabetes and higher baseline fasting serum insulin.[9]
- A proposed mechanism for the improvement in glycaemic control is that caloric restriction leads to glycogen depletion in muscle and liver. Restriction of carbohydrate leads to lipolysis and the formation of ketone bodies by the liver. Together these responses lead to reductions in hepatic glucose output via inhibition of gluconeogenesis and reduced glycogenolysis. Circulating ketone bodies have also been shown to increase satiety.[10] Weight loss and reduction of fat deposits in the liver, muscle, pancreas and perivisceral space lead to increased insulin sensitivity, which along with improvements in dynamic insulin secretion and reduced hepatic glucose output lead to reductions in blood glucose levels.[11]
- Most international guidelines on diabetes management recommend weight loss with calorie restriction. Recommendation for the use of VLEDs over other diets is limited by the lack of long-term efficacy data. However, there are no studies indicating long-term safety concerns.

Recommendations for Management

a) Patient Suitability

Most patients with a BMI >27kg/m^2 that have T2DM are suitable for treatment with OPTIFAST VLCD as part of an overall program that emphasises the importance of ongoing weight maintenance.

Patients who are obese with T2DM and associated diabetic complications such as microalbuminuria, non-proliferative retinopathy, obstructive sleep apnoea, non-alcoholic fatty liver disease and diastolic cardiac dysfunction are suitable for weight management with the OPTIFAST VLCD Program.

Patients with more severe complications such as proteinuria >1g/d, eGFR <60 or risk of fluid balance complications need to be carefully monitored (creatinine, eGFR, electrolytes, nutritional markers, nitrogen balance) while on a VLED.

Use of OPTIFAST VLCD Program Intensive Level is often initiated prior to bariatric surgery in obese patients with T2DM (as well as those without T2DM) to reduce the liver size and so improve accessibility and visibility for laparoscopic procedures. It is likely that other metabolic markers improve preoperatively with OPTIFAST VLCD and may assist with reduction of perioperative complications.

Many patients are reluctant to initiate insulin management despite having high blood glucose. If OPTIFAST VLCD Program Intensive Level is used in this setting a considerable improvement in glycaemic control usually occurs within 1–2 weeks. If not, other hypoglycaemic measures should be instituted. Thus, patients with poor glycaemic control who are starting a full OPTIFAST VLCD Program should monitor their blood glucose levels regularly and be reviewed within 1–2 weeks of initiating the OPTIFAST VLCD Program.

b) Adaptations to OPTIFAST VLCD Program

Patients on insulin or sulphonylureas need to be careful to avoid hypoglycaemia and, if possible, simplifying the insulin regimen or changing to an oral agent that does not increase basal insulin secretion is recommended.

Unless glycaemic control has been poor, the insulin or sulphonylurea dose should be reduced on commencement of a VLED and glucose levels should be closely monitored. It is recommended that if the HbA1c is less than 7.5%, the insulin and sulphonylurea dose should be reduced by 50%.

On the full OPTIFAST VLCD (Intensive Level), patients on basal bolus insulin usually do not need pre-meal insulin bolus doses and require a reduction in the basal dose. A practical recommendation is to initially halve the basal dose and review frequently with self-blood glucose monitoring. When only 1 or 2 meals are replaced with OPTIFAST VLCD the bolus dose may only need to be reduced or withheld prior to these meals.

Patients on twice daily pre-mixed insulin (breakfast and dinner) who are starting the Intensive Level of the OPTIFAST VLCD Program, are often best managed by changing their insulin regimen to a single basal insulin injection at half the dose of their usual total insulin dose.

c) Contraindications and Precautions

Antihypertensive treatment may need to be adjusted while on a VLED as blood pressure often falls. Thus in these patients, blood pressure should be regularly monitored. Lipids often improve markedly following weight loss so it may be possible to reduce doses of lipid-lowering medications following a VLED.

The OPTIFAST VLCD Program is not recommended for people with diabetes with normal or low weight, women with diabetes associated with pregnancy or people with cystic fibrosis-related diabetes.

Case Study

Erica has had T2DM for 7 years with associated obesity, complicated by hypertension, dyslipidaemia, macroalbuminuria (0.6g/d) with stage III chronic kidney disease (eGFR 55ml/min/1.73m^2) and sleep apnoea (on CPAP). She is on metformin, a sulphonylurea, maximum dose ACE-Inhibitor, a calcium channel blocker and a statin.

Six months ago, her HbA1c was 9% and she was commenced on twice daily mixed insulin. She is now on 60 units BD. Her HbA1c has improved to 7.6% but she has gained 10kg and her BMI is now 40kg/m^2. She has now developed gastro-oesophageal reflux and is finding physical activity very difficult largely because of her weight.

Together with her doctor she decides to go on the OPTIFAST VLCD Program. In anticipation of a fall in her glucose levels she is changed to a basal insulin at a dose of 60 units nocte and is able to achieve target blood glucose readings. With increasing weight reduction, her glucose levels start to fall to 4–5mmol/L and her insulin dose is progressively reduced so that by the time she has been on the OPTIFAST VLCD Program for 6 weeks she is no longer requiring any insulin. Her blood pressure also falls and she stops the calcium channel blocker.

After having been on the VLED for 3 months she starts having 1 regular healthy evening meal and replaces breakfast and lunch with an OPTIFAST VLCD product. She gradually weans off the OPTIFAST VLCD products over the next month and is extremely happy with her progress. She has managed to reduce her weight by 14kg so that her BMI is now 35kg/m^2. She no longer requires insulin and her dose of sulphonylurea has been halved. Her ability to exercise is much improved and she is intent on maintaining her weight by walking regularly and eating a healthier diet. She realises that she will need to monitor her weight regularly and if she finds it increasing, in consultation with her doctor, she would consider recommencing the OPTIFAST VLCD Program either to replace all meals or 1–2 meals daily.

Medications used in Type 2 Diabetes

Table 1: Medications used in Type 2 Diabetes – considerations and potential benefits with the OPTIFAST VLCD Program

Medication	Mode of Action	Effect on Weight	Important Considerations with OPTIFAST VLCD	Potential Benefits with OPTIFAST VLCD
NON-INSULIN AGENTS				
Metformin	Lowers blood glucose levels by reducing the amount of glucose produced and released by the liver, and by increasing insulin sensitivity	Modest loss or neutral	Monitor renal function – cease if eGFR <30 or unstable renal function	Minimal risk of hypoglycaemia
Sulphonylureas	Stimulate insulin secretion from the pancreatic beta cell	Increases	Risk of hypoglycaemia if dose not adjusted; Increases insulin secretion (obesogenic)	May allow control of glycaemia
Glitazones (Thiazolidinediones) TZDs	TZDs make your body produce new fat cells, and those cells are actually more sensitive to insulin – that is, they allow insulin to do its job	Increases	VLED may potentiate the risk of reduction in bone mineral density with this agent	Minimal risk of hypoglycaemia
Acarbose	Slows down the action of certain chemicals that break down food to release glucose into the blood	Modest loss or neutral	Unlikely to be additional benefit due to low carbohydrate intake on VLED	May be of benefit in non-replacement meals or maintenance phases
SGLT-2 inhibitors	SGLT2 inhibitors work by preventing the kidneys from reabsorbing glucose back into the blood	Modest loss	Can lower blood pressure; Risk of the rare event of normoglycaemic ketoacidosis if insulin deficient*	Minimal risk of hypoglycaemia
DPP-IV inhibitors	Block the action of DPP-4, an enzyme which destroys the hormone incretin	Modest loss or neutral	Avoid if patient at high risk of pancreatitis	Minimal risk of hypoglycaemia
GLP-1 analogues	Copy, or mimic, the functions of the natural incretin hormones in your body that help lower post-meal blood sugar levels	Modest loss	Avoid if patient at high risk of pancreatitis	Minimal risk of hypoglycaemia; May assist with adherence to VLCD
INSULIN AGENTS				
Basal		Increases	Risk of hypoglycaemia; Reduction in dose likely necessary if on Intensive Level	May allow control of glycaemia
Mixed Insulin		Increases	Risk of hypoglycaemia; generally, not recommended with a VLED, consider changing to basal +/- bolus insulin	May allow control of glycaemia
Basal Bolus		Increases	Risk of hypoglycaemia; Usually a reduction in dose of both basal and bolus component is required	May allow control of glycaemia

* There is a rare risk that SGLT-2 inhibitors may cause normoglycaemic ketoacidosis if the patient is insulin deficient. Other factors that can also contribute to ketoacidosis include; dehydration, intercurrent illness and severe energy restriction. Therefore, it is important that patients on SGLT-2 inhibitors & OPTIFAST VLCD are adequately hydrated and instructed that if they become unwell, particularly if they experience nausea, vomiting and/or abdominal pain they stop the SGLT-2 inhibitor and seek urgent medical advice.

All diabetic medications should be reviewed prior to commencing the OPTIFAST VLCD Program and be supervised by a qualified healthcare professional.

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Pregnancy, Infertility and IVF

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Review of Clinical Evidence

- In overweight or obese women with anovulation, weight loss has been encouraged to increase fertility. Thus, a VLED such as OPTIFAST VLCD may be suggested to patients with obesity-related infertility. The impact of prior VLED use on a subsequent pregnancy outcome is difficult to assess as controlled clinical trials are not available.
- There has been a single case report demonstrating a successful pregnancy with intrauterine insemination (IUI) 5 months after following a 6-week VLED intervention in a woman with obesity, diabetes and hypertension.[1] Despite this, weight loss using a VLED should be attempted prior to any effort to achieve pregnancy and in clinical practice, contraception is advised while on the Intensive Level (3 x OPTIFAST meals/day) of the OPTIFAST VLCD Program.
- In regard to IVF treatment, there has been some suggestion of unsatisfactory IVF outcomes in a group of overweight and obese patients using a very low-calorie diet for a short period before and during IVF.[2,3] It is therefore recommended to cease the use of a VLED six weeks prior to embryo insertion for those that are undergoing Assisted Reproductive Technology (ART).[3]
- As there is no evidence to indicate that very low energy diets are either beneficial or even safe during pregnancy they are contraindicated.

Recommendations for Management

a) Patient suitability

Women planning pregnancy should achieve a healthy body weight well in advance of planned conception.

A VLED-based program such as the OPTIFAST VLCD Program may be useful prior to conception to assist with weight loss and increase fertility in overweight or obese individuals with anovulation. However caution should be exercised and the VLED should be ceased 6 weeks prior to conception. Following the VLED period individuals should be advised to maintain their weight with a healthy balanced diet and regular physical activity in the lead-up to conception.

In the event that a VLED program is recommended prior to embryo insertion during IVF, the VLED should be ceased 6 weeks prior.

b) Adaptations to OPTIFAST VLCD Program

The OPTIFAST VLCD Program may be used to achieve a healthy body weight and normalise metabolism prior to pregnancy. At around the time of conception and during pregnancy women should maintain healthy balanced nutrition, regular physical activity and avoid excessive weight gain.

A modest weight loss using a healthy balanced diet that is low in saturated fat and refined carbohydrates, together with regular physical activity improves fertility in obese women, particularly those with polycystic ovary syndrome (PCOS).

c) Contraindications and Precautions

VLEDs should not be used during IVF or pregnancy and should be ceased 6 weeks prior to embryo insertion for those that are undergoing Assisted Reproductive Technology.

Whether OPTIFAST VLCD is useful as part of a meal replacement strategy in relation to pregnancy, fertility and IVF remains to be determined.

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Hypertension

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Review of Clinical Evidence

There is no specific literature concerning the use of VLED therapy and adverse events in patients with hypertension, however it is known that weight loss can assist in lowering blood pressure.

This has been demonstrated with VLED therapy including with OPTIFAST VLCD.[1,2]

Recommendations for Management

a) Patient Suitability

There is no contraindication for patients with uncomplicated hypertension in using the OPTIFAST VLCD Program, however some caution is needed to avoid the possibility of orthostatic hypotension.

b) Adaptations to OPTIFAST VLCD Program

VLED therapy can produce a rapid weight loss, and orthostatic hypotension associated with negative energy balance and weight loss may occur. Excessive falls in blood pressure may require temporary modification to antihypertensive therapy.

Altered hydration and hypotension are particularly likely to occur if patients are taking diuretics, angiotensin converting enzyme inhibitors, and angiotensin blockers, or combinations of these, to treat hypertension.

Diuretics should be stopped at the beginning of the VLED because VLEDs themselves have a diuretic effect. Other medication for hypertension should be continued and tapered according to blood pressure values. Blood pressure should be monitored regularly throughout the program.

It is important to warn patients about the symptoms of orthostatic hypotension and advise an adequate intake of water.

Blood pressure should be monitored and the dosage of hypotensive medications altered if needed. Hot weather and exercise may exacerbate the hypotensive effect.

It should not be assumed that sustained fall in blood pressure will occur with weight loss and blood pressure requires long-term monitoring.

c) Contraindications and Precautions

Caution should be used when using OPTIFAST VLCD in patients taking antihypertensive medications. Hydration should be maintained and temporary changes to medications may be necessary to avoid hypotensive episodes. Long-term reductions in blood pressure have been reported.[3]

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Hepatic Disease

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Review of Clinical Evidence

Liver Disease

- Obesity and the metabolic syndrome predispose to non-alcoholic fatty liver disease (NAFLD), which can progress through steatohepatitis to cirrhosis and liver failure.
- NAFLD aggravates the damage caused by other hepatotoxic conditions including alcohol and Hepatitis C. Generally, weight loss improves NAFLD, but evidence is limited, of low quality, and some therapies may exacerbate liver disease.
- Obesity surgery has probably given us the best evidence regarding significant weight loss.
- Jejuno-ileal bypass, a major malabsorptive procedure, was abandoned for a number of reasons including strong evidence that it caused liver damage, cirrhosis and death in a significant minority of cases. The more recent malabsorptive procedure, the bilio-pancreatic diversion, has a mixed effect on the liver. A sub-group of patients characterised by those with very rapid and extensive weight loss, diarrhoea-steatorrhoea or low plasma albumin levels tended to have deteriorating liver histology, and cirrhosis and liver failure have been reported.[1] Weight loss induced by modern bariatric surgery, including the laparoscopic sleeve gastrectomy, laparoscopic adjustable gastric banding and the roux-en-Y gastric bypass, have improved liver histology and not been associated with liver morbidity.[2]
- Rapid weight loss induced by a VLED can induce a transient and reversible (2–6 week) rise in liver enzymes.[3]
- One observational study with paired biopsies found some subjects developed portal inflammation and fibrosis with extensive VLED-induced weight loss. Those likely to develop portal changes had greater steatosis initially, greater loss of liver fat and more rapid weight loss.[4]

Gallstones

- The risk of developing gallstones is greater in obese subjects. The relative risk is 5–6 times that of the background population at a BMI of 40kg/m^2. Rapid weight loss, such as that induced by a VLED increases the risk of developing gallstones, and gallstone-related disease. The addition of a teaspoon of vegetable oil or added fat to the VLED products assists in reducing the risk of gallstones.
- Identified risk factors for developing gallstones during weight loss are a relative loss of weight greater than 24% of initial body weight, a rate of weight loss greater than 1.5kg per week, and a very low calorie diet with limited fat.[5]

Recommendations for Management

a) Patient Suitability

Weight loss is recommended for obese patients with liver disease, however rapid weight loss is not recommended for patients with advanced liver disease.

b) Adaptations to OPTIFAST VLCD Program

In those with known hepatic disease or dysfunction the OPTIFAST VLCD Program may be commenced at one of the lower levels i.e. Active 2 or Active 1 and be stepped up toward to the Intensive Level progressively over weeks while monitoring liver enzyme levels.

c) Contraindications and Precautions

VLEDs are not recommended for those patients with the following conditions:

- Portal hypertension
- Liver failure
- Cirrhosis
- Symptomatic gallstones
- Past history of pancreatitis

For patients with liver dysfunction or known liver disease the doctor should monitor liver enzyme concentrations.

Patients with asymptomatic gallstones should be made aware of the symptoms of gallstone complications. It is important to advise the patient to use vegetable oil with the vegetable or salad intake to regularly contract the gall bladder and thus reduce the risk of further gallstone formation.[6]

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Notes

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OPTIFAST VLCD is for the dietary management of obesity and must be used under the supervision of a healthcare professional.

BENEPROTEIN is a food for special medical purposes specifically formulated for medical conditions where nutritional needs cannot be met by diet modification alone. Must be used under the supervision of a healthcare professional.

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