CHAPTER 16 LUNG TRANSPLANTATION

D. Hickling, A. Matson, M. O'Driscoll & C. Rawcliffe

Lung transplantation is a treatment option which can offer a survival benefit and improved quality of life for some people with end stage cystic fibrosis (CF) [738]. Optimising nutrition prior to lung transplantation can help to improve perioperative and post lung transplant survival outcomes [739-741].

There are 5 lung transplant units in Australia and New Zealand performing lung transplantation for people with CF – Fiona Stanley Hospital (WA), The Alfred Hospital (VIC), The Prince Charles Hospital (QLD), St Vincent's Hospital (NSW), and Auckland City Hospital (NZ). The Alfred Hospital hosts the Nationally Funded Centre for Paediatric Lung Transplant. Each unit is staffed by a interdisciplinary team specialising in transplantation. In Australia 31% (658 transplants) of bilateral lung transplants in adults (1992-2015) were for CF [742]. CF-related lung disease is the leading indication for lung transplantation in children [743-745] with over 50% of lung transplants in children 6-10 years and 69% for children 11-17 years being for CF [746].

In CF, lung transplantation is considered when life expectancy is poor despite optimisation of both medical and surgical management. The International Society for Heart & Lung Transplantation (ISHLT) 2014 Consensus document for the selection of lung transplant candidates [747] recommends that transplantation be considered for suitable people with CF who have a 2-year predicted survival of <50% and who have functional limitations. Timing of referral for lung transplant can be indicated by a number of factors, including worsening nutritional status despite supplementation, as outlined in the ISHLT 2014 Consensus document.

It is important for the CF and lung transplant teams to maintain open communication channels, with clear referral guidelines and pathways [2,3].

Early referral for lung transplant is essential to patient education and to allow adequate opportunity for modification of risk factors associated with worse outcomes [748]. Appropriate timing for referral of paediatric patients may be indicated for children on maximal medical therapy with a poor quality of life and a short predicted life expectancy [747].

The ISHLT consensus document also lists both absolute and relative contraindications to lung transplantation. Nutrition related contraindications include [747]:

ABSOLUTE CONTRAINDICATIONS:

- Class II or III obesity (body mass index (BMI) ≥35kg/m^2)
- Current non-adherence to medical therapy or a history of repeated or prolonged episodes of non-adherence to medical therapy

RELATIVE CONTRAINDICATIONS:

- Class I obesity (BMI 30.0-34.9kg/m^2), particularly truncal (central) obesity
- Progressive or severe malnutrition
- Severe, symptomatic osteoporosis
- Sub-optimal management of diabetes mellitus

International registry data reports the median survival time post lung transplantation in people with CF as being 8.5 years for adults [749]and 5.2 years for paediatric patients [746]. International Kaplan-Meier survival rates for adult lung transplant recipients with CF (January 1990 to June 2013) are 84% to 1 year, 48% to 9 years and 34% to 15 years [749].

16.1 Pre-transplantation

Pre-transplant care should be overseen by the local CF team [2]. Once a person with CF is listed for transplantation, close liaison between the CF team and the transplant team is essential [2].

Disease Aetiology

From a nutrition perspective, the period before transplantation is critical. Individuals with end-stage CF lung disease are at risk of significant weight loss as energy expenditure is raised. This is secondary to pulmonary sepsis, declining respiratory function and increased work of breathing associated with infective exacerbation [750]. Poor appetite and

difficulty eating/drinking due to shortness of breath can further impact a patient's ability to meet energy requirements. Mortality in underweight CF transplant recipients (BMI < 18.5 kg/m^2) is higher than in those of normal weight [19,739-741]. Increased mortality has been reported in underweight patients (BMI < 18.5 kg/m^2) on the lung transplant waitlist [19]. Class II Obesity (BMI ≥35kg/m^2) has also been found to contribute to the risk of mortality after transplant in both CF and non-CF recipients [739,741]. Of note some studies have not found an increased risk of mortality in people with CF who are underweight, when compared to a normal weight [751].

Assessment

Prior to transplantation listing, a thorough assessment by an interdisciplinary team specialising in lung transplantation is required. Aspects considered by the transplant team include respiratory function, rate of decline in lung function, age, sex, nutrition status, presence of other CF complications (CF-related diabetes status and management, osteoporosis, GOR, liver and renal function), quality of life, social support, adherence and the individual with CF's choice. A history of repeated non-adherence to medical therapy, or current non-adherence that is perceived to increase the risk of non-adherence post-transplantation, is an absolute contraindication to transplantation [747]. Chronic graft rejection due to non-adherence is particularly prevalent in adolescent patients and therefore needs to be addressed during transplant assessment [747]. For all patients, health outcomes post-transplantation may be negatively impacted by poor medication adherence [750,752].

The process of determining patient suitability for lung transplantation should include a comprehensive nutritional assessment, ideally by an experienced dietitian. Relevant information provided by the referring CF centre will enhance nutritional assessment.

Factors to take into consideration in handover, and in transplant nutrition assessment, are detailed in the sections (diet and clinical) below.

DIET

- Recent diet history and pancreatic enzyme replacement therapy (PERT) record
- CF-related diabetes: consider insulin/carbohydrate intake and ratio, as relevant
- Nutrition support: type, amount, mode (oral or enteral), frequency of use, tolerance, PERT dosage
- Adherence to recommendations regarding nutritional support

CLINICAL

GENERAL CONSIDERATIONS

- Check for nutrition impact symptoms: appetite, nausea, vomiting, early satiety.
- **Medications:** review micronutrient supplementation and adherence, gastrointestinal medications (prokinetics, anti-emetics, proton-pump inhibitors, acid suppressing agents and aperients), and complementary alternative medications.
- **Bone Health:** screening for osteoporosis should be undertaken prior to lung transplant [747,753] as severe and symptomatic osteoporosis is a relative contraindication for transplant [747]. This also allows earlier intervention to improve BMD status.
- **Comorbidities:** review control of comorbidities that may contribute to worsening nutritional status prior to transplantation.
    - **Gastrointestinal system** – GOR, Bowel habits, history of diarrhoea, constipation, distal intestinal obstruction syndrome (DIOS), infections with *clostridium difficile*, heightened risk of colorectal cancer (including previous investigations).
    - **Endocrine system** – CF-related diabetes: ensure recent screening (if not screened in last 12 months this will need to be addressed) and note date of diagnosis, duration of CF-related diabetes, management (frequency of BGL monitoring, insulin regimen and adherence, hypoglycaemia management, trend of HbA1c). Some transplant programs may have specific HbA1c targets.

ANTHROPOMETRY AND BODY COMPOSITION

- ISHLT guidelines outline severe or progressive malnutrition as a relative contraindication to lung transplant, therefore nutrition status needs to be assessed.
- Height, weight and BMI (including highest and lowest weights and recent weight history); local programs may have specific BMI or percentile targets for both children and adults.

- While the Subjective Global Assessment tool [754] has not been validated in the CF population, it may be one of many tools used to determine nutritional status.
- Where available: body composition, skinfold measurements, bone densitometry (DEXA), bioelectrical impedance analysis. See Chapter 5.

BIOCHEMICAL AND LABORATORY DATA

The following parameters should be reviewed:

- Fat-soluble vitamin levels and history
- Iron studies
- Oral glucose tolerance test. See Chapter 12 for diagnostic levels
- Liver and renal function
- Lipid profile

PSYCHOSOCIAL CONSIDERATIONS

- Supports to optimise food access and meal preparation
- Social and emotional issues affecting adherence to dietary advice and /or CF-related diabetes management
- Consider the impact of exercise and physical activity prescribed by physiotherapy on the individual's overall energy balance/requirements

Intervention

Prior to lung transplantation clinical care aims to optimise the patient's nutritional status [755]. Maintenance of lean body mass is a priority[756]. Aggressive nutritional support (via enteral feeding) may be required to counteract the rising energy requirements in patients with end stage CF lung disease. The option of transplantation and the need to meet specific nutrition-related or weight targets may assist the individual to prioritise nutritional improvements.

The following strategies should be considered:

- Optimising energy intake [755], progressively using nutritional strategies (behavioural, oral and enteral) See Chapter 6.
- Optimising efficacy of PERT. See Chapter 10.
- Optimising diabetes management if HbA1c >7.5%, as improving glycaemia may improve weight gain. See Chapter 12.
- Supplement fat soluble vitamins, as required with the goal of correcting to the normal reference range. See Chapter 9.
- Correcting mineral deficiencies (sodium, calcium, iron). See Chapter 9.
- Optimising nutrition management of gastrointestinal and hepatobiliary co-morbidities if present. See Chapter 11.
- Addressing nutrition-related factors contributing to low BMD and consider need for additional medical therapy prior to transplantation, including suboptimal calcium intake, vitamin D and K status. See Chapters 8 and 13.

Monitoring & Evaluation

Nutritional status should be assessed regularly while patients are on the transplant waiting list [755]. Good communication between both the treating CF team and the lung transplant team is essential.

16.2 Post-Transplantation

Post-transplant care is generally coordinated by the specialised transplant unit. Contact with the local CF team may be important to some individuals with CF to ensure that CF-specific medical problems can be addressed [2].

Nutritional management in the immediate post-operative period should focus on attaining adequate protein and energy intake [178]. Energy needs are increased in order to offset catabolism secondary to surgery, and anti-rejection

medication [178]. Some people will regain their appetite and eat well soon after surgery as breathing becomes easier, taste sensations improve, bowel function normalises and mobility improves. However, others experience anorexia and poor oral intake due to post-transplantation medications, taste changes, constipation, nausea and vomiting [178].

Aetiology of Post-Transplant Considerations

Post lung transplant the following nutrition-related issues may occur, and are important to consider:

BONE DISEASE (Chapter 13)

Reductions in bone density commonly occur following lung transplantation [753,757]. Corticosteroids and other medications that are required post-transplant may exacerbate pre-existing osteoporosis [753]l Osteoporosis is common post lung transplant and it appears to be more severe than that associated with heart, kidney, liver or bone marrow transplants [646]. The pathogenesis of osteoporosis post-transplantation appears to be multifactorial, with cumulative steroid doses being the major contributing factor.

BOWEL MANAGEMENT

Constipation and distal intestinal obstruction syndrome (DIOS) are common post lung transplant [758], with reported rates of up to 20% [563,564]. DIOS is particularly common in the early post-operative period [564,758,759]. Prevention and early treatment of constipation and DIOS is important and contributing factors to consider are outlined in Chapter 11. People with a history of previous major abdominal surgery, meconium ileus in infancy or DIOS require close monitoring as they are at greater risk of developing post-transplantation DIOS [564,760]. Early post-transplant post-operative pain management with opioids is also a contributing factor [759].

Clostridium difficile colonisation or recurrent infection is common in older CF patients and in the setting of immunosuppression, *clostridium difficile* colitis may lead to severe consequences [758,761]. People with CF are 2-3 times more likely than non-CF lung transplant recipients to develop *clostridium difficile* in the first 12 months post-transplant [758,762].

DELAYED GASTRIC EMPTYING

Delayed gastric emptying has been found in people with end stage CF both prior to [598] and post lung transplantation [598,760,763-765]. A number of factors can contribute to gastroparesis symptoms post-transplant, including pre-existing gastroparesis, surgical vagal disruption (at time of transplant or during fundoplication), diabetes management [597] and choice of immunosuppressant. Cyclosporin has been linked with slower gastric emptying while tacrolimus has prokinetic properties [597,766]. Gastroparesis symptoms can impact on a patient's ability to meet their nutritional requirements.

DIABETES (Chapter 12)

The post-transplant immunosuppressive regimen, which includes high doses of prednisolone and tacrolimus, cyclosporin or sirolimus, places individuals with CF at risk of developing new onset diabetes after transplant (NODAT) [767-769], or exacerbating existing CF-related diabetes [178]. This is secondary to both insulin resistance and insulin deficiency [178,767-769]. Prednisolone contributes to insulin resistance, where tacrolimus has been shown to reduce both insulin production and sensitivity [767-769].

NODAT rates have been reported as 20-32% of all patients post lung transplant [748,770-772]. In the CF population without pre-existing CF-related diabetes, NODAT has been reported to develop in 25-38% of individuals [769,771]. One Australian study found diabetes in 68% of CF lung transplant recipients, 63% of these patients had diabetes prior to transplant, with an overall NODAT incidence of 25% [771]. NODAT can be transient and is most common in the early period post lung transplant, with rates found to decrease to 19-20% at 12 months [748] and 17% at 24 months [770]. Corticosteroids, although reduced in dose in the 12 months post-transplant, are rarely ceased in lung transplant recipients and can contribute to NODAT persistence.

Irrespective of lung transplantation, CF-related diabetes is associated with a worse lung function, more chest infections, overall poorer nutrition and increased mortality [773]. The development of NODAT has been associated with an adverse impact on survival and an increased risk of graft rejection and graft loss, as well as an increased incidence of infectious complications [768]. In a retrospective case-control study including 25 CF patients almost all developed hyperglycaemia following lung transplant, but patients with diabetes prior to lung transplant had more complication related admissions to hospital and a higher mortality rate [774].

DRUG-NUTRIENT INTERACTIONS

Medications used to prevent complications, such as antibiotics, immunosuppressants and anti-fungal medications, can have marked side effects, including taste changes, nausea, vomiting and diarrhoea. Mycophenolate is commonly included in post-transplant immunosuppressant regimens and is associated with adverse gastrointestinal events, including diarrhoea [775-777]. A literature review showed adverse gastrointestinal events as the main reason for dose reduction, interruption and discontinuation of mycophenolate [778].

Organ transplant recipients are at a high risk for drug-nutrient interactions due to multiple medication regimens. Some herbal supplements have immunostimulant properties and modulate platelet aggregation. This may contribute to post-transplant complications or graft dysfunction [779]. Given the significance of these interactions, it is important to discuss the use of all supplements with the treating team, including a pharmacist, to avoid potential interference with a patient's immunosuppressant therapy. All supplements should be confirmed as being clinically indicated and confirmed with the treating team, including pharmacy, to ensure no drug-nutrient interactions before being commenced.

One of the most significant examples of drug-nutrient interactions involves grapefruit juice, which significantly increases the absorption of many currently available immunosuppressants, increasing the risk of drug toxicity [780]. Cyclosporin is highly lipophilic and sub-optimal enteral absorption may account for low bioavailability in people with CF [780]. Lung transplant physicians may recommend one to two low dose pancreatic enzyme capsules be administered with each dose of medication to facilitate absorption. However, PERT may have no effect on cyclosporin bioavailability and higher doses of immunosuppression drugs may be needed by people with pancreatic insufficiency in order to achieve therapeutic concentrations [781].

Tacrolimus and cyclosporin may also be associated with hyperkalaemia. This is not always in the presence of acute or chronic renal failure and occurrence is not limited to early post-transplant, but may occur later. Hypomagnesaemia is a common side effect of tacrolimus and cyclosporin, therefore magnesium supplementation is routinely required from early post-transplant.

GOR (Chapter 11)

Gastrointestinal complications, including GOR, are more common post lung transplantation [542,757,763,764,782-784]. The aetiology of post-lung transplant related GOR is poorly understood, with possible causes being vagal injury, delayed gastric emptying, oesophageal dysmotility and oesophageal sphincter relaxation. GOR may contribute to a decline in lung function before and after lung transplant [542,785]. GOR can also be present as "silent reflux" where patients are asymptomatic. GOR has been found to be highly prevalent in lung transplant recipients and significant reflux has been identified as a risk factor for bronchiolitis obliterans syndrome (BOS) [786-788].

REDUCED IMMUNITY AND FOOD BORNE ILLNESS

Immunosuppressive therapies make organ transplant recipients more vulnerable to infections. It is widely accepted that these infections could potentially come from food contaminants, such as bacteria, viruses and parasites. Specific data on the risk associated with food-borne infections for Australian lung transplant recipients (with or without CF) is not available. However, review articles provide detail on the potential sources of foodborne and waterborne pathogens post-transplant, which may include Listeria, Salmonella, Crytosporidium, Giardia and Toxoplasma Gondii [789-792]. The World Health Organisation also lists immunosuppressed patients as being at risk of waterborne pathogens [793].

While listeriosis remains relatively rare across all populations, internationally increased rates have been found in transplant recipients [794-796]. A review by Silk et al. [794] showed case reports of foodborne listeriosis in immunocompromised patients. A French study of all listeriosis cases from 2001 to 2008 showed an increased risk of listeriosis in transplant recipients, with incidence rates of 7.91, compared to 0.39 per 100,000 overall incidence, but that transplant patients had the lowest fatality rate (6%) amongst risk groups assessed [795]. A Spanish study of all listeriosis cases in transplant patients from 1995 to 2007 found the same rate (0.12%) of listeriosis in lung transplant compared to all transplant types (0.12%). This study reported that while listeriosis in solid organ transplants is uncommon, it can cause a high mortality rate (26.7%) [797].

An Australian review of waterborne gastroenteritis outbreaks from 2001 to 2007 reported that while they are uncommon, the majority of drinking water sources are tank water or bore water related, with most common pathogens confirmed as salmonella, campylobactor, giardia or cryptosporidium species [798]. The study acknowledges most incidents are likely not reported, due to no medical treatment being sought [798]. The World Health Organisation Guidelines for Drinking Water Quality note that while rainwater is often as safe as drinking water, there are issues with pathogens and bacteria from the way it is stored, temperature of storage and where the water is collected from which is putting immunosuppressed individuals at risk [793].

Assessment

There are a number of potential nutrition related diseases and symptoms post-transplant that require assessment, and/or intervention and monitoring.

DIET

European and US recommendations for energy requirements in CF vary from 110-200% of energy needs for a healthy population [78,799]. In view of the lack of CF-specific evidence, energy and protein requirements immediately post-lung transplantation are based on recommendations for general surgical and other types of transplant patients. Use of surgical requirements provides a baseline for establishing minimum intakes (125-145KJ/kg, 1.2-1.5g/kg protein in adults). Nutritional status at time of surgery needs to be considered as malnourished patients are likely to have higher requirements than their well-nourished counterparts.

PERT

Recommendations for assessment explored in Chapter 10 are applicable post-transplant.

HYDRATION

It is important to check patient's usual home water supply, those with tank or bore water access will need further education regarding water safety.

COMPLEMENTARY ALTERNATIVE MEDICATIONS

Due to drug-nutrient interactions, complementary alternative medications are not recommended post-transplant, unless clinically indicated and confirmed with the treating team.

CLINICAL

GASTROINTESTINAL SYMPTOMS

Gastrointestinal symptoms should be regularly monitored, as per usual clinical assessment. In addition to this, due to the risk of gastroparesis directly post-transplant and/or post fundoplication, it is important to explore potential symptoms of gastroparesis, including nausea and/or vomiting, poor appetite, early satiety and poor volume tolerance. See Figure 16a for management algorithm and severity classification [800].

BONE DISEASE

Recommendations for assessment explored in Chapter 13 are applicable post-transplant. Regular BMD screening post-transplant will assist in identifying changes in BMD status (Chapter 13).

BOWEL MANAGEMENT

Assessment and stool samples in cases of diarrhoea post-transplant are recommended to assess for c.difficile infection [758,761]. Recommendations for assessment of constipation and DIOS explored in Chapter 11 are applicable post-transplant.

DIABETES (Chapter 12)

In the immediate post-transplant period blood glucose levels increase acutely, as a surgical stress response, necessitating post-surgical insulin in all patients. The potential for substantial weight gain in the first 1-2 years post-transplant likely contributes to insulin resistance in patients [801].

Factors to consider when assessing risk of NODAT:

- Age
- Ethnicity
- Weight history (consider history of obesity)[801]
- Family history of diabetes [801]
- Medications:
    - Immunosuppressant regimen (cyclosporin, tacrolimus and/or sirolimus) [770]
    - Dosage of corticosteroids (considering both basal doses and periods of prednisolone pulses at which time intermittent diabetes may occur) [801]

While optimal timing for testing for NODAT is yet to be determined, studies have indicated between 3-12 months is appropriate [748,801,802], with OGTT recommended at 3-6 months post-transplant [801]. This is after the immediate post-transplant period of higher immunosuppressant regimens, where transient diabetes may be present [748,802]. Regular fasting plasma glucose can be used to screen for impaired fasting plasma glucose levels. Bloom & Crutchlow [801] also recommend annual OGTT post-transplant due to the poor sensitivity of fasting plasma glucose when compared to OGTT.

In patients with known diabetes, regular BGL monitoring, three to four times daily is recommended.

BIOCHEMICAL AND LABORATORY DATA

FAT SOLUBLE VITAMINS

Monitoring should continue regularly post-transplant, a minimum of annually. See Chapter 8. Practice may vary across sites.

LIPIDS

Annual review is recommended post-transplant.

Intervention

DIET AND ENTERAL NUTRITION

Oral nutrition therapy post-lung transplantation can usually commence post-operatively following extubation. Early initiation of normal food or enteral nutrition after transplantation is strongly encouraged [755]. Intake can advance as tolerated to a regular diet, with accompanying PERT if pancreatic insufficient [178,756].

Enteral nutrition should be considered for patients with longer ventilation periods. The American Society for Parenteral and Enteral Nutrition (ASPEN) *Guidelines for Nutrition Support in the Critically Ill* support the use of enteral nutrition, when feasible within 24 hours of major surgery [803]. Supplementary enteral feeding may also be indicated if oral intake is insufficient to meet requirements [520]. Enteral feeding may be ceased when a patient can consume 65-75% of their requirements orally, the addition of oral supplements may be used to meet their overall requirements [520]. Some drugs used post-transplant require consideration regarding their interactions with food and may impact timing of enteral feeding regimens. See drug nutrient interactions below. Refer to Chapter 10 for considerations of PERT with enteral feeding.

The European Parenteral and Enteral Nutrition (ESPEN) *Guidelines for Surgery and Transplantation* [755] recommend the initiation of early nutrition support in the perioperative period, without delay:

- If it is anticipated that the person will be unable to eat for more than 7 days peri-operatively (even in people without obvious undernutrition).
- In people who cannot maintain oral intake above 60% of recommended intake for more than 10 days.
- Via enteral route except for the following contraindications: intestinal obstructions or ileus, severe shock, intestinal ischemia.

Consider pre-transplant nutritional status in decision-making about post-transplant nutrition support.

DELAYED GASTRIC EMPTYING

Prokinetics and dietary modification are recommended for the management of gastroparesis [597,598]. Treatment should include optimising glycaemic control (where relevant).

In terms of dietary modifications, fat and fibre are known to delay gastric emptying, so limiting these sources may be beneficial [597]. In cases of gastroparesis, digestion of liquids is usually preserved, therefore a liquid/pureed diet can improve tolerance to meet energy requirements [597].

In addition to dietary modification, prokinetics should be considered to improve gastric emptying and gastroparesis symptoms [597]. Long-term prokinetic use has been shown to safely improve delayed gastric emptying in lung transplant patients [804]. Whilst treatment with antiemetic agents will address nausea and vomiting, these mediations will not result in improved gastric emptying [597].

Awareness of drug interactions is vital as a number of prokinetics interact with transplant medication regimens, including domperidone with azithromycin, and erythromycin with tacrolimus/cyclosporin.

If oral intake is insufficient in an individual with post-transplant gastroparesis, then post-pyloric feeding (jejunostomy or naso-jejunal) should be considered [597]. Indications for enteral nutrition in cases of gastroparesis include unintentional loss of 10% or more of the usual body weight during a period of 3-6 months, and/or repeated hospitalisations for refractory symptoms [597]. Post-pylorus botox (botulinum toxin) injections, and surgical interventions including gastric pacemakers and pyloroplasty are relatively new treatment alternatives for severe gastroparesis, not resolved with diet and motility agents alone [597].

Post-pylorus botox (botulinum toxin) injections, and surgical interventions including gastric pacemakers and pyloroplasty are relatively new treatment alternatives for severe gastroparesis, not resolved with diet and motility agents alone [597].

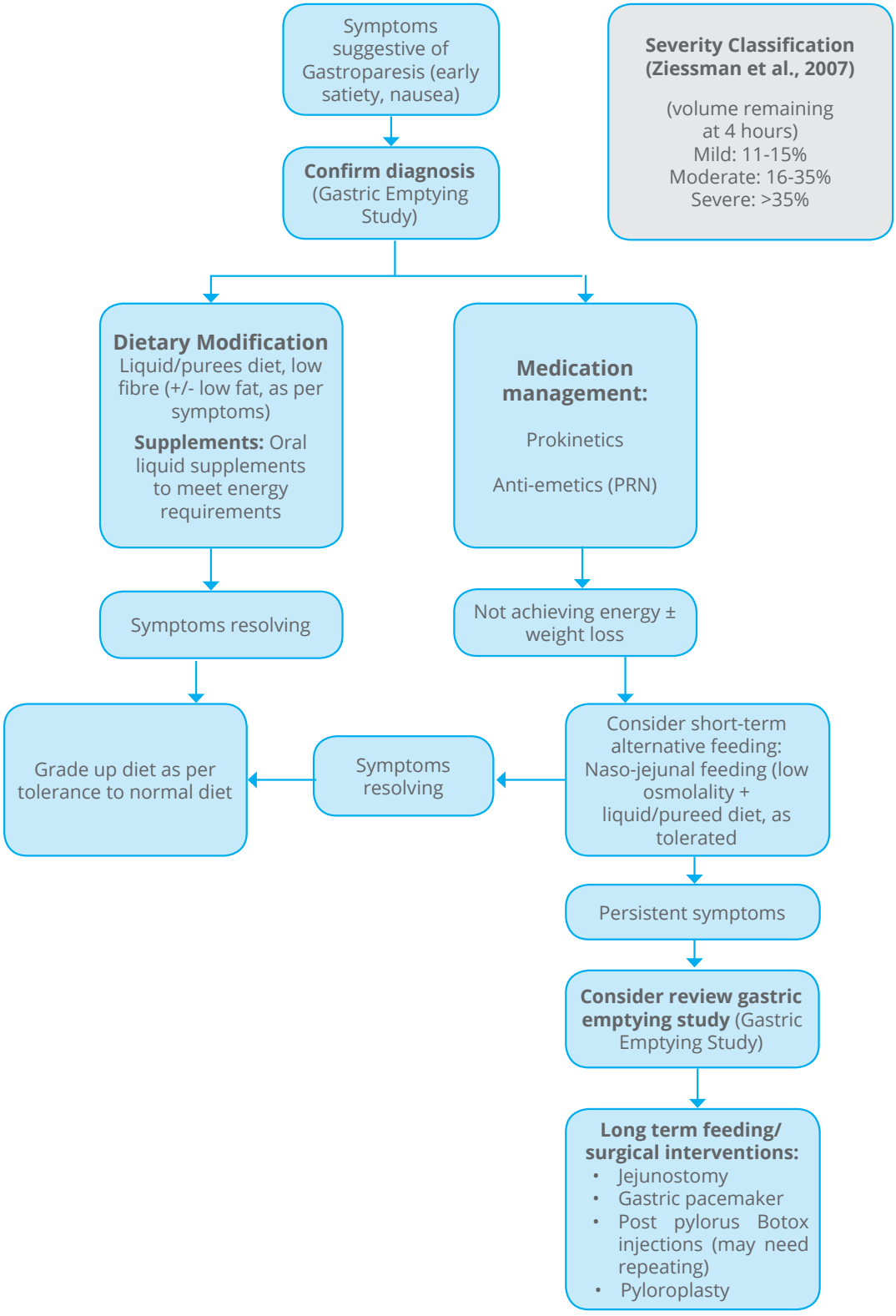

Figure 16a. Gastroparesis management algorithm for CF lung transplant (adapted from Camilleri et al., 2013)

DRUG NUTRIENT INTERACTIONS

Posaconazole suspension (liquid form), an anti-fungal medication, must be taken with a high fat meal to improve absorption [805] and achieve an adequate level; whereas posaconozole tablets can be taken with or without food [806].

Fasting times for oral medications should be considered when planning enteral feeding regimen timing. Intermittent feeding with breaks for oral or enteral tacrolimus administration and pre/post fasting is therefore more appropriate than continuous feeds. Regular electrolyte monitoring is important, and avoidance of a high potassium diet may be indicated in the presence of hyperkalaemia as explained in Aetiology [805,807]. Tacrolimus should be taken on an empty stomach either one hour before or two hours post food [807].

DIABETES

Management in the post-transplant period typically requires insulin and is predominantly due to the effect of prednisolone and tacrolimus. Three monthly monitoring of HbA1c is important. Regular review with the endocrine team is required with insulin doses needing to be adjusted with reduction in steroid dosage, adjustments in tacrolimus dosing and with intercurrent pulse steroids to manage rejection episodes or increase in steroids to manage episodes of infection.

Target HbA1c for NODAT is 6.5%, with a fasting BGL target of <6mmol/L, and post-prandial target of <8mmol/L [768]. This aligns with UK targets for type 1 diabetes of 6.5% or 48mmol/mol [641]. Specific targets for post-lung transplant patients with CF have not been established (see Chapter 12 for CF-related diabetes targets). Further research into NODAT in people with CF may alter HbA1c or BGL targets, however until then, an individualised approach to establishing HbA1c targets is recommended for CF patients with diabetes post-transplant, with consideration of hypoglycaemia and lifestyle factors [768]."

HYDRATION

Ensure patients maintain adequate hydration (up to 3-4L/day in adults, if required) as renal function may be adversely affected by immunosuppressive medications.

BOWEL MANAGEMENT (Chapter 11)

Where diarrhoea is persistent, and nutrition-related causes have been excluded, it is recommended to raise concerns with the treating lung transplant team to consider potential medication causes, such as mycophenolate. Recommendations for intervention for constipation and DIOS are explored in Chapter 11 and are applicable post-transplant.

REDUCED IMMUNITY AND FOOD BORNE ILLNESS

In Australia and New Zealand, there are no consistent dietary guidelines or food safety information provided to transplant recipients. In the absence of a standardised approach, discrepancies in the content and delivery of dietary education have been noted between centres [808,809].

If a food borne illness is contracted, it has been suggested that transplant recipients may experience more rapid onset of symptoms than the general population which can lead to severe dehydration, organ failure, sepsis or even death [789]. As a result, education on food safety with advice to avoid foods with a high bacterial load is generally recommended for solid organ transplant recipients. There is no current published evidence to support the efficacy of any food safety measures or dietary restrictions in reducing the risk of food-borne illness in lung (or other organ) transplant recipients. Similarly, there is no evidence regarding the duration that dietary restrictions are required. This may explain why food hygiene is not universally prioritised by patients.

Bore water and tank water that is untreated and not screened frequently for bacterial pathogens should be avoided due to risk of contamination [792]. Untreated water should be brought to rolling boil for 1 minute to kill all pathogens. Solar/ultraviolet water disinfection are a low-cost disinfection option for the treatment of water. Disinfection sanitises the water and reduces the risk of gastrointestinal infection. UV disinfection is particularly effective at removing cryptosporidium from water, whereas cryptosporidium is extremely resistant to chlorination alone. Further treatment at the point of consumption (reverse osmosis or filtration) may be applied to ensure better quality of drinking water and reduce health risks [793].

Useful resources for patient education can be located at:

- Queensland Health Nutrition Education Materials Online: "Safe Eating for Immunocompromised Patients" and "Food Safety" (https://www.health.qld.gov.au/nutrition/nemo_oncol)
- New South Wales Food Authority: (http://www.foodauthority.nsw.gov.au/foodsafetyandyou/life-events-and-food/low-immunity
- Victorian Better Health: https://www.betterhealth.vic.gov.au/health/healthyliving/food-safety-when-cooking

GOR

Anti-reflux surgery, such as a fundoplication, post lung transplantation, has been found to be safe and to result in an improvement in the rate of change in FEV_1 post lung transplant [785]. Two studies have shown improved long-term survival following anti-reflux surgery [783,810]. Some Australian lung transplant centres routinely perform 24 hour pH studies from three months post-transplant, when post-operative gastroparesis is likely to have resolved.
Texture modification can be required post fundoplication due to dysphagia-like symptoms. Education on early post fundoplication dietary modification should be provided by the treating dietitian. Short term nutritional supplementation may need to be considered to avoid weight loss. Chapter 11 provides a further summary of nutritional management strategies and on the medical management of GOR (including the use of PPIs for less severe GOR).

BONE HEALTH

In addition to adequate oral intake of calcium, prophylactic vitamin D and calcium supplementation can be recommended in patients with diagnosed osteopaenia or osteoporosis either in pre-lung transplant screening or post lung transplant [811,812]. Routine BMD is recommended to be undertaken 12 months post-transplant, annually thereafter for those with declining BMD, or every 2 years for patients with stable BMD. Patients with a T score <-1.5 require anti-bone resorptive medication (on the basis of steroid therapy) and a diet with sufficient calcium to meet RDI. Adequate vitamin D (>50nmol/L levels) [813] and weight-bearing exercise will also assist in maintaining bone health. See Chapter 13 for further information.

Monitoring & Evaluation

Long-term nutritional monitoring and advice is recommended for all transplant recipients [755]. After the initial post-surgical period and achievement of a healthy weight, routine nutritional management should be re-established.

ENERGY

After lung transplantation, energy requirements decrease as the work of breathing is reduced and infective exacerbations are fewer. An improved appetite due to the effects of anti-rejection medications and improved overall well-being assist in a person's ability to meet requirements orally. Dietary energy intake may need to be reduced in order to maintain a BMI of between 20 and 25 kg/m^2 in adults and normal growth trajectory in children. Dietary counselling to normalise eating habits and achieve a varied diet is important, particularly for those who have relied heavily on oral supplements or enteral feeding prior to transplant, and those with identified body image concerns.

Nutritional needs can change over time, particularly for those with a decline in health status, including longer-term post-transplant. In periods of infection or clinical deterioration, either acute or chronic, poor appetite or GI symptoms may contribute to increased nutrition requirements, reduced intake and/or weight loss. People with CF may require dietary modification including increasing energy intake either short-term or longer-term to prevent the development of malnutrition, including consideration of enteral feeding. This may include nasogastric feeding, or the consideration of insertion/reinsertion of a gastrostomy tube. Refer to Chapter 6 for nutritional interventions.

REMOVAL OF GASTROSTOMY

People with CF who have relied on supplementary enteral nutrition via a gastrostomy tube prior to lung transplantation can usually reduce the use of enteral nutrition as oral intake increases and nutritional status improves and if clinical status is satisfactory. Gastrostomy removal should be discussed between the individual with CF and the lung transplant team and assessed on an individual basis. Removal should be planned when the patient is clinically stable and able to consume adequate oral intake to maintain their goal weight without use of the gastrostomy [294,814,815]. The potential need for nutrition support via gastrostomy in the future should also be considered [814].

Prior to gastrostomy removal, it is recommended to seek a surgical and/or gastroenterological opinion regarding management [814]. Upon removal, the gastrostomy is likely to close within 2-7 days. Patients with tracts that do not heal within one week or with output from their stoma site should be referred for further medical and/or surgical input [814]. There is little to no evidence regarding permanent gastrostomy removal and closure in adults and/or CF lung transplant. However, clinical experience supports formal closure in patients with longstanding gastrostomies. Paediatric research in renal transplant has shown that gastrostomies in-situ for longer than one year are more likely to require surgical closure, with spontaneous closure more likely in those present for less than 12 months [816]. Other studies have supported that gastrostomies placed for over 11 months are less likely to spontaneously close [817,818].

DELAYED GASTRIC EMPTYING

Patients should be monitored for symptoms of gastroparesis, including early satiety, poor appetite, nausea and vomiting. If symptoms are present then a gastric emptying study may be indicated to formally diagnose gastroparesis.

DIABETES

Similarly to CF-related diabetes, regular self-monitoring of BGLs and HbA1c is recommended for all patients with NODAT, refer to Chapter 12.

VITAMINS AND MINERALS

Similar to energy needs, vitamin needs post-transplantation are often reduced. Serum vitamin A and E levels have been observed to be significantly higher in this population group, even after supplementation has ceased [819]. Factors possibly influencing vitamin levels include a decrease in pulmonary exacerbations, drug interactions and impaired retinol metabolism or increased hepatic synthesis of retinol binding protein [60,819]. Early monitoring of vitamin levels initially post-transplant (at 3-6 months post-transplant) will indicate when supplementation can be reduced or ceased, with ongoing annual review thereafter. Local protocols may vary in terms of cessation of vitamin replacement and timing of monitoring. Vitamin D supplementation may be continued in the presence of and/or for prevention of osteopaenia/osteoporosis, as per Chapter 8.

GOR

Monitoring for symptoms of gastroparesis post fundoplication and early intervention if identified is recommended to maintain nutrition status - see figure 16a. While symptoms are common in the first 3 months post fundoplication, the majority of patients' symptoms resolve by 1 year [597]. Monitoring for symptoms of gastroparesis post fundoplication and early intervention if identified is therefore recommended to maintain nutrition status.

DIOS

DIOS can recur later post-transplant [766]. Therefore, ongoing prevention strategies as detailed in Chapter 11 remain applicable post-transplant.

NUTRITION-RELATED LONG-TERM COMPLICATIONS

Increasing medical complications are being encountered with improved survival post-transplantation. Early recognition of these complications, and therapy directed to prevent these complications, may lead to reduced morbidity and mortality in patients who have undergone lung transplant. These complications have been comprehensively summarized for further information [820].

If other post-transplant complications or new unrelated conditions emerge which require additional dietary management or restriction of one or more dietary components, an individualised nutrition management plan should be developed which takes into account requirements for CF, lung transplant and the concurrent conditions. Examples include renal disease and malignant conditions. Input from both the transplant team and other teams including the dietitian may be required.

Lipids are routinely monitored post- transplant and if hyperlipidaemia is identified then dietary interventions are indicated (Chapter 7). With the achievement of a healthy BMI, ongoing education for healthy eating choices should be encouraged, including consideration of appropriate dietary fat sources and limiting saturated fat intake.

CHRONIC KIDNEY DISEASE

Chronic Kidney Disease (CKD) is a common complication after non-renal solid-organ transplantation. The risk of CKD is influenced by many factors, some of which have a direct impact on how such patients are treated in the pre-, peri- and post-transplantation settings. The most common cause of renal failure is calcinuerin inhibitor (CNI) nephrotoxicity [821], CNI medications forming part of patient's immunosuppressant regimen. Monitoring of renal function, and diet modifications to manage impaired renal function should be on a case by case basis and in consultation with specialist renal services. Evidence based guidelines for nutritional management of chronic kidney disease in Australia and New Zealand are available [1].

BONE HEALTH

Due to the ongoing requirement for medications contributing to osteoporosis, including tacrolimus and corticosteroids, regular BMD testing is recommended as outlined in the Interventions section of this chapter [753,759].