



Dietary Guidelines Post Kidney Transplant: Is This the Missing Link in Recovery and Graft Survival?

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The physiology of a transplanted kidney is affected from the moment it is separated from the donor. The risk of complications arising from surgery are highly associated with ischemic-reperfusion injury (IRI) due to the effects of hypoxia and oxidative stress during the procurement, preservation and reperfusion procedures. Hypoxia promotes the formation of reactive oxygen species (ROS) and it seems apparent that finding ways of optimising the metabolic milieu for the transplanted kidney would improve recovery and graft survival. Studies have demonstrated the benefits of nutrition and antioxidant compounds in mitigating the disturbance of energy supply to cells post-transplant and at improving long-term graft survival. Particularly in patients who may be nutritionally deficient following long-term dialysis. Despite the high incidence of allograft failure, a search of the literature and grey literature reveals no medical nutrition therapy guidelines on beneficial nutrient intake to aid transplant recovery and survival. This narrative review aims to summarise current knowledge of specific macro and micronutrients and their effect on allograft recovery and survival in the perioperative period, up to 1-year post transplant, to optimise the metabolic environment and mitigate risk to graft injury.

Keywords: kidney transplantation, nutrition guidelines, graft survival, post kidney transplant care, diet post transplant

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INTRODUCTION

The physiology of a transplanted organ is affected from the moment it is separated from the donor. The risk of complications arising from surgery are highly associated with ischemia-reperfusion injury (IRI) due to the effects of hypoxia and oxidative stress during the procurement, preservation and reperfusion procedures [1, 2]. As hypoxia promotes the formation of reactive oxygen species (ROS), it seems apparent that finding ways of improving antioxidant levels would optimise the milieu within which the transplanted organ is placed.

Nutrition is broadly accepted as playing a role in optimizing patients' health pre- and post-transplant, and requirements for different nutrients change significantly as kidney function declines. Renal insufficiency is associated with significant changes in electrolyte handling and cellular balance of sodium, potassium, phosphate and calcium, all of which are biologically vital. Dietary restriction contributes significantly to reducing kidney disease progression in more advanced disease [3, 4]. Dietary restrictions limit the options of access to whole foods rich in these minerals, such as vegetables, dairy and nuts, which can cause patients to increase their intake of ultra processed foods (UPF). UPFs typically contain additives, preservatives, artificial sweeteners, and emulsifiers, with

limited dietary fibre, all of which impact the biodiversity of the microbiome [5]. Kidney transplant recipients (KTR) are therefore at risk of nutritional deficiencies by the time they receive their donor organs, affecting antioxidant status, and potential imbalance in the gut microbiota, with increased production of uremic toxins [4, 6, 7].

The Role of the Gut Microbiome

Evidence suggests that gut microbiota play an important role in the metabolism, storage, and expenditure of energy and nutrients, and play a pivotal role in host immunity, and metabolic function [8, 9]. The integrity of the gut microbiome therefore affects the host's ability to absorb nutrients and regulate immunity [9].

Dysbiosis of intestinal flora is associated with complications in KTR, and many patients experience dysbiosis particularly in the first month post-transplant [10–12]. The causes of dysbiosis are multifactorial and can be assigned to the use of preparative regimens prior to transplantation as well as prophylactic antibiotics and immunosuppressant drugs [13]. Dysbiosis may influence graft outcomes, causing acute rejection, infection, renal fibrosis, and modification of drug metabolism [8, 14, 15].

Given the ability of the microbiota to influence isoimmunity and drug metabolism, data suggest that modifying the microbiota could contribute to more targeted immunosuppressive and post-transplant complication therapies, to improve graft survival and patients' quality of life (QoL) [13, 16, 17]. Diet modification particularly the inclusion of prebiotic and probiotic foods is beneficial in altering an abnormal microbiota to produce the host's own antimicrobial substances, thereby improving immune function and graft survival [18, 19]. These prebiotic foods contain high amounts of fibre which serve as a food source for many of the gut microbiota, and a commensal partnership exists between the host and these bacteria [20].

While there is consensus on the increased risk of foodborne infection, especially in the first 6 months post-transplant, recommendations for the avoidance of consuming fresh fruit and vegetables vary across national guidelines [21, 22]. Several studies have questioned whether these protective diets provide any significant benefit in terms of infection rates, compared to a non-restrictive diet and may contribute to nutritional deficiencies [23, 24]. A common metric of gut health is the diversity of microbial species, and any acute changes can modify this composition within just 24 h [25, 26]. There is currently a lack of relative evidence referring to the microbiota in renal transplantation, with most studies conducted on animals [8, 27]. Research is therefore needed to understand the implications of chronic dysbiosis and its effect on graft survival in humans.

As nutrition is a vast subject, we acknowledge that this review does not cover all aspects of nutrition that might affect individual patients. We therefore focus specifically on nutrients that are highly monitored during ESKD to determine their effect on allograft health post-transplant and highlight the relevance of continued monitoring particularly in the critical early (up to 1 year) period post post-transplant.

MATERIALS AND METHODS

Published data were searched using the Medline National Library of Medicine, MEDLINE and Embase. No date restriction was applied, to broaden the search, however only English language papers were included. Search terms used included Diet, Nutrition Therapy, Dietary Guideline*Intervention* Nutrition*, Policy, AND Transplant*, Renal, Kidney Transplantation. 68 papers were identified, and after initial review of titles and abstracts for relevance, three duplicates were removed. A secondary review revealed no papers focused specifically on dietary guidelines post kidney transplant, although 20 covered individual macro and micronutrients which served as thematic insight for this paper. A grey literature search within the major national and international Kidney transplant organisations was also conducted to confirm whether any nutrition guidelines were available for post-transplant support. None were found (Figure 1). A narrative review, adopting a systematic synthesis of the available evidence of the individual macro and micronutrients was conducted with all papers reviewed by authors. Thematic analysis was identified by the primary author and confirmed by author 2 and 3. These themes will be discussed here.

RESULTS

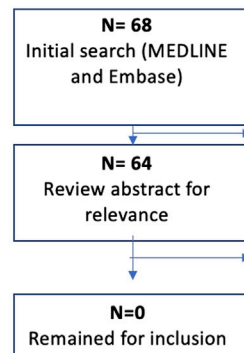
Our findings show a paucity of specific dietary recommendations for KTR, and the studies currently available focus on single nutrient intakes, and not on the overall eating pattern. Considering that individuals do not typically consume nutrients in isolation it is challenging for single nutrient interventions to demonstrate conclusive effects and modifying dietary patterns as a whole may present a more realistic alternative or provide a complementary approach to single-nutrient interventions. We discuss these individual nutrients here, and demonstrate how the composition of the diet, particularly one that focuses on lower carbohydrate intake may be of increased relevance to graft survival.

Macronutrients: Protein

Protein requirements change during various phases post-transplant. The first few weeks post-transplant are characterized by increased nutritional demands due to the associated stress of surgical insult to the body and the high doses of immunosuppressive medications [28]. During this critical phase large glucocorticoid doses cause accelerated protein catabolism to achieve positive Nitrogen balance and improve wound healing while conserving muscle [29, 30]. There are currently no agreed guidelines on a recommended protein intake for KTR, although a review by Chadban et al [29] recommends around 1.4 g/kg/day protein intake during the first 4 weeks post transplantation to reverse negative Nitrogen balance and increase muscle mass. This was also found protective in reducing the risk of increased fat mass and muscle loss up to 1 year post transplant. Once patients are on a maintenance diet, research suggests a distinction be made between diabetic and

Search Terms:

Diet, Nutrition Therapy, Dietary Guideline*Intervention* Nutrition*, Policy, AND Transplant*, Renal, Kidney Transplantation; Graft Survival

Search Strategy:

N= 4
: Duplicates (3); Prospective Study (1)

N= 64

Removed: Specific micronutrient interventions (20); Weight Loss guidance (12), CKD/ESRD (7); Other (6), CVD Prevention (5); Diet Behaviour Change (4); Microbiome (2); Diet Intervention (2); Surgery/Drugs (2); Body Composition (1); Diet Compliance (1); Cost (1); Virology (1);

Grey Literature searched:

American Transplant Association, *American Society of Transplantation* British Transplant Society, KDIGO Clinical Guidelines (2020), National Kidney Foundation; National Institute of Clinical Excellence (NICE), (2024). Scenario: Management of chronic kidney disease; Renal Association (2010). *The Organ Procurement and Transplant Network/United Network for Organ Sharing (OPTN/UNOS) database.*

Findings: The Literature search revealed no official dietary guidelines for Post Kidney Transplant recovery or graft survival.

FIGURE 1 | Literature review strategy: post kidney transplant dietary guidelines.

non-diabetic KTR patients, advocating slightly higher protein requirements in diabetic patients (0.8–0.9 g/kg/day vs. 0.6–0.8 g/kg protein/day) based on the beneficial effects of protein in stabilising blood glucose [31, 32].

KTR frequently suffer with severe fatigue, which ultimately affects quality of life (QoL), and the role of protein in muscle repair, energy metabolism and neurotransmitter production (such as dopamine and serotonin) are well documented [33, 34]. A cross-sectional study, involving 730 stable KTR [median age 58 years (IQR 48–65), 57% male] with a mean protein intake of 82.2 ± 21.3 g/d were assessed to examine the association of protein intake with fatigue and QoL. Moderate and severe fatigue were present in 254 (35%) and 245 (34%) of KTR. Higher protein intake was significantly associated with lower risk of moderate fatigue (OR 0.89 per 10 g/d; 95%CI 0.83–0.98, $p = 0.01$), severe fatigue (OR 0.85; 95%CI 0.78–0.92, $p < 0.001$) and was associated with higher physical component summary scores for QoL (β 0.74 per 10 g/d; 95%CI 0.39–1.09, $p < 0.001$) [35]. This suggests that higher protein intake is independently associated with lower risk of moderate and severe fatigue and better QoL in KTR. It is important to note that enhanced protein intake alone, without resistance training may limit this benefit, due to the anabolic stimulus that exercise provides in muscle maintenance [36].

Several studies have however found that restricting dietary protein in KTR with chronic allograft nephropathy or chronic rejection may be beneficial, with respect to kidney function; however, further research is needed to identify the magnitude of benefit and a safe level of intake for this patient group [37, 38].

Carbohydrates

Metabolic disorders after kidney transplantation are common, and various dietary approaches have been studied regarding their effects on co-morbidity progression such as weight gain, hypertension, hyperlipidaemia, and insulin resistance [39]. Exposure to immunosuppressive medications such as glucocorticosteroids can cause or worsen preexisting hyperglycemia and weight gain [40–44], and regulating blood glucose has favourable downstream implications in slowing kidney disease progression [45–47].

As carbohydrates are the major contributor to post prandial hyperglycemia, increasing evidence highlights the benefits of very low-carbohydrate (ketogenic) diets to reduce inflammation, maintain euglycemia and weight, by improving satiety, reducing hyperglycemia and hyperinsulinemia. [48–50]. These diets are generally cautioned against for individuals with impaired kidney function, partly due to concerns about increased protein intake, which is associated with hyperfiltration and potentially, a decline in kidney function [51–53]. While classification of these diets differ greatly within the literature, differences are based on the proportion of total daily energy from carbohydrate and/or absolute carbohydrate intake [54]. Dietary analysis of very low carbohydrate studies usually report daily protein intake from 0.6 g/kg to 1.4 g/kg; which is below the high protein threshold (≥ 2.0 g/kg) believed to be of concern [55, 56].

The available literature on very low carbohydrate diets in KTR is scarce, although several studies recommend it as a therapy for preventing or assisting in recovery from ischemic and traumatic injuries [57–59]. The extensive topic of ketone

body metabolism is beyond the scope of this article, but in brief, when following a keto diet (KD) or during fasting, fatty acids are relocated from adipocytes to liver cells, and transformed into the Acyl-CoA form, then transported to the liver to produce ketone bodies, which provide an alternative form of ATP energy [60]. Since disturbances in the energy supply of cells during ischemia cause a transient interruption of normal blood flow to the kidney, there is an increase in oxidative stress and inflammation [61]. Ketone bodies have demonstrated nephroprotective effects in IRI, due to their ability to suppress the concentration of proinflammatory factors, such as tumour necrosis factor alpha, interleukins including IL-6; IL-1 β , IL-18, IFN, and decreased expression of the NF- κ B and MCP-1 which induce the expression of various proinflammatory genes [57, 62]. The natriuretic and diuretic effect of the KD may also provide additional kidney protection by helping to alleviate sodium retention and improve systemic and glomerular blood pressure [63, 64].

As there is currently no agreement on isocaloric comparisons recommending a specific carbohydrate intake for KTR, clinicians are challenged to provide risk assessments and guidance [65]. While the KD implies an increased intake of fat, this definition is not standard across studies, and it is important to distinguish between the types of fat and their ratios in the overall diet, which will be discussed in the section below [66].

Fats

There are currently no specific recommendations for dietary fat intake post kidney transplant, and patients are advised to follow the recommendations for the general population [31]. There is also no consensus on what the optimal ratio of n-6: n-3 polyunsaturated fats (PUFA) should be. Few studies investigate Essential Fatty Acid (EFA) deficiency in KTR, although low intakes have been attributed to renal hypertension, mitochondrial activity disorders, Cardiovascular Disease (CVD), type 2 diabetes, and decreased resistance to infection [67, 68].

Inflammation is part of the body's immediate response to injury or infection, and it begins the immunological process of eliminating pathogens and toxins to repair damaged tissue [69]. Although inflammation is a normal response, when it occurs in an uncontrolled or inappropriate manner excessive damage and disease to the affected tissue(s) can ensue. Dyslipidaemia is a known risk factor for CVD and evidence suggests that KTR have significantly lower serum content of potentially beneficial Polyunsaturated Fatty Acids (PUFA) compared to CKD patients not on dialysis [70]. PUFAs help regulate the antioxidant signalling pathway and modulate inflammatory processes. Both Omega 6 and Omega 3 play a key part in balancing inflammation to achieve homeostasis. Several sources suggest that humans evolved on a diet that had a ratio of omega-6 to omega-3 EFA of about 1:1; whereas today, Western diets have a ratio of approximately 10:1 to 20:1 [71, 72]. While pro-inflammatory omega 6 plays an important part in host defence, by creating a hostile environment for microbes and later by initiating tissue repair, recovery, and maintenance of

homeostasis, prolonged (unresolved) inflammation can cause tissue damage and metabolic changes [73]. By contrast, Omega -3 (n-3) have shown improved renal and cardiovascular prognosis, and protective benefits against inflammation and overall mortality in KTR, due to their antithrombotic, anti-inflammatory, and antiarrhythmic effects [74–77].

In one study investigating the effects of n-3 PUFA supplementation on kidney allograft function and lipid profile, 60 long-term, first time KTR were assigned to 2 groups: a CON group ($n = 28$), who continued with their usual diet, and the DIET group ($n = 32$), who followed an n-3-PUFA rich diet for 6 months to investigate changes in n-3 PUFAs intake; the n-6: n-3 PUFAs ratio, systemic inflammation markers, and renal function. At 3 and 6 months the DIET group had significantly higher n-3 PUFA levels and a markedly lower n-6: n-3 PUFA ratio than baseline. This group also had reduced systemic inflammation with decreased plasma total cholesterol, triglycerides, C-reactive protein, and decreased interleukin (IL)-6. While eGFR remained unchanged, this group also experienced 50% reduction in proteinuria and microalbuminuria compared to baseline [78].

Further clinical studies are needed to confirm beneficial ratios of n6: n3, particularly in the initial weeks and months post-transplant, to gauge the positive effects of controlled inflammation as part of the healing process, and the protective effects of n3 in renal function long term.

Micronutrients

Sodium

The literature regarding sodium intake and hypertension in KTRs is scarce and gaps in knowledge still exist on the exact amount needed to optimize graft outcomes and reduce the risk of CVD. This is mostly due to the lack of clarification on the best methods to measure sodium intake; and the often-complex co-morbidities experienced by KTR. The 2012 KDIGO Clinical Practice Guideline recommend a salt intake to <90 mmol (<2 g)/day of sodium (corresponding to 5 g of sodium chloride) for CKD patients with high blood pressure, the same as for the general population [79]. The supporting evidence for this recommendation is of low quality as it references only an adequate intake for adults aged 19–50 years, “based on meeting sodium needs of apparently healthy individuals.” This infers that the guidelines are relevant to those who are moderately active, live in a temperate climate and have no metabolic diseases or compromised kidney function, which does not apply to KTR.

A 2024 literature review by Afsar et al investigating sodium intake and renal transplantation showed continued inconsistencies [80]. Some studies found no relationship between sodium intake and hypertension [81–83] while others found a positive association, although these studies were conducted on rats [84, 85]. Contrasting views also found no association between sodium intake and proteinuria/albuminuria in graft function [86] while others showed a positive association [87, 88].

Numerous studies highlight the effect of insulin on renal sodium transport and metabolism; and demonstrate that

TABLE 1 | Variations in potassium recommendations across the general and CKD population.

US food and nutrition board (IOM, 2005) [101]	The World Health Organization (WHO, 2012) [102]	K/DOQI, National Kidney Foundation (2000) [103]	Comprehensive review by Kalantar-Zadeh et al., (2017) [104]
4.7 g (120 mmol) per day in healthy adults	3.9 g (100 mmol) per day or at least 90 mmol/day (3,510 mg/day) in healthy adults. No specific guidelines for kidney disease (CKD stage 1–5)	Unrestricted potassium intake in non-dialysis dependent patients with CKD stage 1–5 In hemodialysis patients, up to 2.7–3.1 g/day and in peritoneal dialysis patients up to 3–4 g/day	Intake of 4.7 g/day in the early stages of CKD without risk of hyperkalaemia, but a dietary potassium restriction of less than 3 g (77 mmol) per day in CKD patients prone to hyperkalaemia

individuals with arterial hypertension have reduced insulin sensitivity and hyperinsulinemia, compared to subjects with normal blood pressure [89–91].

As a mineralocorticoid, insulin plays an important role in sodium balance, particularly in conditions of elevated circulating plasma insulin concentrations. Plasma insulin stimulates sodium reabsorption by the distal nephron segments, causing hyperfiltration and a rise in intra-glomerular pressure [64]. As carbohydrates are the major contributor to post prandial hyperglycemia and subsequent insulin secretion, it seems logical that to achieve sodium balance and insulin homeostasis it is necessary to modify the diet, by substitution of carbohydrates with lower carb alternatives [45, 92].

Prospective long-term, randomised controlled studies of the effect of the KD in KTR are warranted specifically investigating their effect on electrolyte imbalance, hyperfiltration and the downstream effects on allograft function [93].

Potassium

Disturbances of potassium balance is a frequent complication among KTR notably immediately post-transplant, and in those with suboptimal graft function and higher calcineurin inhibitor levels [94, 95]. Despite the high incidence and potential life-threatening implications, consensus on potassium management in KTR is lacking – with post-transplant medications and dietary induced hyperkalemia associated with decreased glomerular filtration rates and impaired sodium delivery in the distal nephron [96]. There is currently a lack of research on the specific consequences of untreated hyperkalemia to KTR, although insights from CKD populations highlight the importance of maintaining normal serum K⁺ concentrations particularly in IRI post transplantation, where cells experience metabolic shifts that lead to the inhibition of sodium-potassium ATPase. This inhibition disrupts ion homeostasis, contributing to increased ROS production and subsequent cellular damage [97]. Potassium also helps regulate the inflammatory response by influencing the activation of immune cells and the release of cytokines. Post transplant K⁺ balance is also vital for cardiovascular and renal outcomes [98–100].

Dietary guidelines for potassium vary greatly across the literature and none are specifically directed at KTR (Table 1). KTR that do experience hyperkalemia are frequently advised to avoid high-potassium plant-based foods, although the associated effectiveness is weak as the bioavailability and metabolism of K⁺ is naturally influenced by the other nutrients consumed

[105–107]. K⁺ from plant-based sources in particular have proved beneficial, as they provide alkali and antioxidant vitamins, trace elements and fibre, which promotes intracellular entry and excretion of K⁺ in stool by increasing faecal volume [108]. As constipation is a frequent symptom in KTR, restricting fibre-rich foods can impact intestinal microbiota composition and increase the risk of metabolic acidosis and inflammation [109–111].

The Influence of Insulin on K⁺ Balance

Multiple compensatory mechanisms are enhanced in CKD to maintain potassium homeostasis. Insulin facilitates the uptake of K⁺ into the cells by activating the Na⁺/K⁺-ATPase pump [112].

In hyperglycemia, elevated glucose leads to osmotic diuresis, causing significant loss of water and electrolytes, including K⁺, resulting in an apparent elevation of serum K⁺ while depleting cellular stores [100]. Studies show that reducing insulin requirements through reduced carbohydrate consumption improves insulin sensitivity which in turn helps to stabilise K⁺ levels [100, 113].

As new onset diabetes after transplant (NODAT) is a common complication occurring in up to 50% of KTR, there is a need for more specific dietary guidelines to optimise insulin balance [114]. Latest guidelines from *KDIGO* (2023) [115] contain no references to dietary recommendations for K⁺, despite commendation that “a healthy diet should be maintained.”

Vitamin D

Numerous studies demonstrate a high prevalence of vitamin D deficiency in KTR, likely due to the effects of immunosuppressive regimens and renal function impairment which affects the ability of the kidneys to convert 25-hydroxyvitamin D [25(OH)D] into 1,25-dihydroxyvitamin D [1,25(OH)₂D] (the active form), and advice that transplant recipients avoid sunlight to minimise the risk of skin cancer [116, 117]. Existing research in KTR highlights the challenges of achieving adequate vitamin D through diet alone and that even after successful kidney transplantation, the activity of 25-dihydroxyvitamin D may not fully normalize [118]. Supplementation is therefore considered more effective, particularly in vitamin D deficiency and excessive immune inflammation [119–121].

Vitamin D has an established function in immunological health, due to its role in calcium homeostasis and restoring mitochondrial membranes by regulating intracellular Ca²⁺ concentrations to decrease ROS production in IRI [122]. Several studies show that low levels of 25(OH) vitamin D can

have deleterious effects on renal allograft health and increase the risk of NODAT [123–127]. Severe vitamin D deficiency is defined as having a serum 25OHD concentration of <10 ng/mL (25 nmol/L) [128]. KDIGO (2020) guidelines for patients with CKD (stage 1–5) suggest that vitamin D deficiency and insufficiency be treated using strategies recommended for the general population. However, a 2015 study of 289 KTR showed that vitamin D status is negatively affected by calcineurin inhibitors (specifically tacrolimus), the most commonly used immunosuppressant, but not experienced in newer mTOR inhibitors, such as sirolimus and rapamycin [117]. Appropriate management of immunosuppression therapy and monitoring of vitamin D status in KTR therefore warrants a more careful and individualised approach compared to the general population.

It is worth noting that studies on vitamin D deficiency in KTR only prove association and adverse outcomes, but not causality. Continuation of the primary disease (i.e., presence of CKD) or a *de novo* disease in the kidney graft could also contribute to proteinuria, worse kidney function and mortality [120]. Larger prospective and interventional RCTs are needed to fully assess the influence of vitamin D on post-transplant outcomes, and the benefits of long-term supplementation.

Vitamin C

KTR are prone to vitamin C deficiency mostly due to the potential remnant long-term effects of dialysis and higher requirements due to the enhanced pro-oxidative and pro-inflammatory status following IRI [129, 130]. Vitamin C is a powerful biological antioxidant which serves as cofactor for several enzymes involved in anti-inflammatory responses, collagen hydroxylation, carnitine and catecholamine biosynthesis [131]. KTR with low levels of vitamin C are therefore at increased risk of poor wound healing and infection immediately post-surgery, and face higher risk of long-term graft failure, due to reduced biosynthesis of collagen and regulatory T cells [132–134].

In a trial assessing Vitamin C in 598 KTR at 3-, 6-, 12-, 24-, and 60-month post-transplantation, Vitamin C deficiency was defined as plasma vitamin C ≤ 28 $\mu\text{mol/L}$ [135]. At all measurement points, KTR had lower plasma vitamin C than potential donors (30–41 $\mu\text{mol/L}$ vs. 58 $\mu\text{mol/L}$), with deficiency ranging from 46% (6-month post-transplantation) to 30% (≥ 1 -year post-transplantation). Dietary vitamin C intake and vitamin C supplementation were associated with lower odds (OR per 100 mg/day 0.38, 95% CI 0.24–0.61 and OR 0.21, 95% CI 0.09–0.44, respectively). This suggests a strong need for vitamin C analysis and potential supplementation, particularly in individuals with delayed graft function.

Supplemental doses of vitamin C of 90 mg to 3 g/day are considered safe, with mild adverse effects, including gastrointestinal disturbances [136]. Studies on long term, high dose supplementation show increased risk of kidney stones (particularly in males with renal insufficiency), due to increased urinary excretion of oxalate [137, 138]. This risk is not replicated in dietary vitamin C due to the saturable absorption of vitamin C from the gastrointestinal tract [139], and the fact that most dietary sources (such as fruit and vegetables) include a high water content.

The Effect of Vitamin C on Delayed Graft Function

In IRI, endothelial cells are activated by the upregulation of pro-inflammatory cytokines. Vitamin C reduces inflammation and endothelial permeability by increasing pro-inflammatory cytokines and phagocytes that contribute to ROS reduction [41, 42, 140, 141]. In a small (19 participant) double-blinded RCT, investigating the effect of vitamin C on delayed graft function (DGF), KTR in the treatment group received an intravenous vitamin C infusion (70 mg/kg diluted in 0.45% saline), with the control group receiving only the dilute solution. The incidence of DGF was not significantly different between the groups after a single dose of vitamin C, although the duration of DGF was substantially shorter in the vitamin C group than the placebo group (7.33 ± 5.68 versus 19.66 ± 0.57 days; $P = 0.02$) [142]. It is important to note that this study did not include the nutrition status of participants and therefore those with higher deficiency rates may have experienced more dramatic outcomes. Additionally, considering the short half-life of the vitamin and the nature of surgical delays, a bolus intravenous dose of vitamin C may have produced more accurate results.

While vitamin C supplements, particularly in the first month post-transplant might provide a safer and more measurable form of intake, the sodium content of vitamin C preparations should be considered, particularly in sodium-restricted patients [70, 136].

DISCUSSION

Our research showed a positive association between poor nutrition status and impact on allograft recovery and survival. There is consensus grounded in evidence that transplant patients have distinct nutritional needs, with many KTR being nutritionally deficient by the time they receive their donor organ, placing them at increased risk of IRI, graft failure and mortality [143, 144]. There are currently limited studies investigating the longitudinal dietary intake of KTR, yet as this group are still considered a subset of patients with CKD they remain at high risk for progression to dialysis and mortality [145]. Our research highlights the difficulty of investigating the effect of individual macro- and micronutrients on allograft health although there is sufficient evident to highlight the negative impact of higher glycaemic diets, due to the downstream effects on renal sodium transport and the effects of hyperinsulinemia on intra-glomerular pressure. While most metabolic disorders post-transplant cannot be modified, diet and obesity are two factors that can safely be manipulated particularly in preventing metabolic disorders such as NODAT and CVD [146]. Obesity is associated with the prevalence and progression of CKD and low carbohydrate diets are recognised as an effective treatment in weight loss [147, 148]. In a context where the prevalence of nutrition-related health conditions is growing, there is an urgent need for nutrition education for physicians, who receive on average less than 24 contact hours of nutrition instruction across the medical degree [149]. Many do not feel comfortable, confident, or adequately prepared to provide

nutrition counselling and this gap in knowledge is contributing to poorer patient outcomes [150, 151].

Findings on PUFA intake demonstrated that the beneficial effects of anti-inflammatory n-3 depend primarily on the dietary n6: n3 ratio. There is no consensus in the literature on what constitutes an optimal ratio, but the benefits of PUFA homeostasis demonstrate that for KTR there is a need for further research particularly to understand whether a higher n-6 ratio in the period immediately post-transplant might enhance immunity, tissue repair and recovery. Longer term maintenance strategies which include a reduction in carbohydrates will naturally have a higher percentage of protein and fat to compensate for the reduced calories [54] and future guidelines are needed to guide patients on optimal composition of dietary fats at various stages post-transplant.

Evidence on protein requirements post-transplant remain contentious and updated research is needed to ascertain a safe level of intake. It is likely that future guidance on protein intake will be based on prevailing renal function and the magnitude of benefit of higher intake to counteract protein catabolism and muscle protein wastage. Literature on hypovitaminosis D in KTR suggest that low sunlight exposure and the accelerated catabolism of vitamin D secondary to glucocorticoid use increases the risk of renal allograft failure and development of NODAT [123]. Evidence suggests that the general population in the UK are deficient of vitamin D, specifically in the winter months [122]. There is therefore a case for individualised monitoring and replacement therapy in this group.

KDIGO clinical guidelines (KDIGO, 2020) recognise that immunosuppression and graft function are only one component of healthcare, yet it makes no mention of the role of nutrition on allograft health and survival. This research demonstrates that monitoring of nutritional status post-transplant should be a clinical priority, with personalised dietary recommendations and provision for self-management strategies.

CONCLUSION

Despite significant medical advances over the last few decades, kidney transplants frequently do not function for the lifetime of the recipient, with more than a third of kidney grafts failing within

10 years following transplantation [152, 153]. It is widely known that nutrition influences all metabolic disease, health and recovery and more specific research is needed on the beneficial effect of targeted nutrition in establishing an optimal metabolic milieu for the transplanted organ to thrive. Clear guidelines which are accessible to patients and clinicians are we suggest, essential since these will provide the missing link in post-transplant care.

AUTHOR CONTRIBUTIONS

Diagnosed with Type 1 diabetes (T1D) at age 11, the lead author (SS) has lived experience of the challenges of managing chronic health through diet. Later diagnosed with end stage renal disease and placed on a dialysis diet, she used this knowledge and experience to write her MSc thesis on the lived experience of the diet and lifestyle challenges of following a highly restrictive dialysis diet. Post kidney-transplant the lack of guidance was starkly evident, making the transition of adapting to managing the health of her new kidney extremely difficult. This lived experience insight has contributed to the detailed analysis and interpretation of the literature included in this review. All authors contributed to the article and approved the submitted version.

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