Nutrition Recalibration in Transplant Recipients: A Phase-Based Metabolic Strategy for Optimizing Graft and Patient Outcomes

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Abstract

Metabolic recovery after solid organ transplantation is dynamic. Traditional nutritional strategies often assume rapid normalization of appetite and metabolic function. However, emerging evidence suggests that transplant recipients undergo a complex metabolic transition. This transition is characterized by insulin resistance, steroid exposure, altered protein turnover, and fluctuating renal function. The concept of "Nutrition Recalibration" incorporates the need for progressive, physiology-aligned nutritional adaptation. This narrative review proposes a mechanistic and clinically actionable framework for nutrition in transplant recipients. Interactions with immunosuppressive therapy, anabolic signalling pathways, and insulin sensitivity are discussed. The Nutrition Recalibration model provides a practical roadmap for clinicians seeking precision nutrition approaches in modern transplant care.

Keywords: Immunosuppression, Insulin resistance, Nutrition, Protein metabolism, Rehabilitation, Transplantation

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Introduction

Advances in transplantation have improved patient and graft survival.[1] However, long-term outcomes are increasingly determined by metabolic health.[2] Transplant recipients experience rapid shifts in energy balance, body composition, insulin sensitivity, and lipid metabolism. This shift is driven by surgical stress, immunosuppressive therapy, and recovery from chronic illness.[2,3] Post-transplant nutritional care has long been focussed on preventing protein-energy wasting.[4] Contemporary evidence suggests that both underfeeding and overfeeding can adversely affect graft and cardiovascular outcomes.[5,6] Excess caloric intake early after transplantation may accelerate adiposity, dysglycaemia, and hepatic steatosis. Inadequate protein intake prolongs sarcopenia and functional decline. These competing risks necessitate a structured, physiology-guided approach.[4-6]

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Metabolic Transition

Post-transplant metabolic recovery should be conceived as a continuum rather than a switch. In the early post-transplant period, recipients continue to experience residual inflammation, insulin resistance, and the catabolic effects of chronic illness. It is simultaneously accompanied by a stage of anabolic repair.[5] This transition is further modulated by immunosuppressive therapies, particularly corticosteroids and calcineurin inhibitors. Both these promote gluconeogenesis, impair insulin secretion, and alter protein metabolism.[3] As graft function stabilizes, there is a progressive improvement in insulin sensitivity, nitrogen balance, and metabolic efficiency.[5,6] This is accompanied by activation of anabolic pathways such as mTOR that support protein synthesis and tissue recovery.[5] However, these changes occur asynchronously, with appetite, energy utilization, and hormonal regulation recovering at different rates. Recognizing this non-linear metabolic trajectory is essential, as it forms the basis for phase-specific nutritional strategies that avoid both undernutrition and metabolic overload during post-transplant recovery. Recognizing this trajectory forms the basis of the Nutrition Recalibration Approach, which advocates progressive dietary evolution aligned with metabolic readiness.

Nutrition Recalibration Framework

The metabolic recovery after transplantation requires progressive adaptation rather than abrupt normalization. Patients often transition from a pre-transplant anorexia and catabolic state to a post-transplant increased metabolic demand. This shift is neither immediate nor synchronized across physiological systems. A sudden escalation to high-calorie feeding during this vulnerable phase may exceed the body's metabolic capacity. This may result in hyperglycaemia, lipotoxicity, and impaired metabolic flexibility.[5-9] A key concept within this framework is the "appetite lag phenomenon," wherein appetite recovery lags the rise in metabolic demand following transplantation.[5,10] Many recipients enter the post-transplant period with

uraemic anorexia, systemic inflammation, and significant muscle wasting. Although surgical recovery and immunosuppression increase energy requirements, appetite often remains blunted initially.[5,10] This mismatch creates a complex nutritional challenge. It predisposes patients to hypocaloric intake if early satiety limits food consumption. Conversely, it leads to a disproportionate intake of refined carbohydrates when easily consumable calories are prioritized.[7-10] Additionally, total caloric intake may become protein-deficient, leading to suboptimal anabolic recovery. Accordingly, nutritional strategies must be anticipatory rather than reactive, gradually aligning dietary composition and caloric load with the evolving trajectory of appetite, metabolic capacity, and graft function to ensure balanced recovery without metabolic overload.

Phase-Based Nutritional Strategy

We propose a phase-based nutrition strategy in transplant recipients, as depicted in Table 1.

Immediate Post-Transplant Phase (0–4 Weeks)

During this phase, patients transition from a pre-existing catabolic state toward early anabolic recovery. However, this shift is incomplete and metabolically fragile.[7-10] The primary goals during this phase are to support wound healing, maintain nitrogen balance, minimize hyperglycaemia, and ensure adequate but tolerable caloric intake. Carbohydrate management is central in this phase and should be guided by the concept of the appetite-carbohydrate mismatch, wherein appetite recovery lags behind metabolic demand.[11] Rather than aggressive caloric repletion, a moderated carbohydrate approach is recommended, typically constituting approximately 45-50% of total energy intake, with an emphasis on low glycaemic index sources. Large, concentrated carbohydrate loads, particularly during post-lunch period when steroid-induced hyperglycaemia is most pronounced, should be avoided5,6. Instead, structured meal timing with consistent carbohydrate distribution across meals helps attenuate glycaemic variability. While dietary fibre improves glycaemic stability and gut health, excessive early use may blunt appetite and reduce overall intake.[12] Therefore, fibre should be introduced judiciously. From a mechanistic standpoint, limiting postprandial glucose excursions reduces insulin surges and counteracts corticosteroid-driven hepatic gluconeogenesis, thereby improving metabolic stability.

Protein nutrition during this phase should follow the principle of "protein quantum and quality," ensuring sufficient anabolic substrate without precipitating early satiety or reduced caloric intake. An initial intake of approximately 0.6–0.8 g/kg/day is appropriate, with gradual escalation as appetite and tolerance improve. Emphasis should be placed on high biological value proteins, including egg white, dairy, soy, lean meats, and legumes, which provide essential amino acids required for tissue repair and immune function.[13] This balanced approach supports early anabolic signalling while mitigating the risk of hypocaloric intake often seen when protein-rich diets suppress appetite disproportionately.

At the level of mesonutrition, amino acid composition, particularly branched-chain amino acids (BCAAs) such as leucine, isoleucine, and valine, plays an important role in modulating muscle protein synthesis through activation of the mTOR pathway and may contribute to improved insulin sensitivity.[14] However, routine or aggressive amino acid supplementation in the immediate post-transplant period is not recommended, especially during phases of high-dose corticosteroid therapy and unstable graft function, as it may increase nitrogen load without proportional anabolic benefit. As renal function stabilizes and metabolic balance improves, a gradual transition toward a balanced amino acid profile through diet becomes more appropriate.

Table-1: Phase-Wise Nutrition Recalibration Strategy in Transplant Recipients.

Phase	Metabolic State	Pathophysiology	Primary Risks	Protein	Carbohydrate	Fat & Micronutrient
Immediate (0–4 weeks)	Catabolic to early anabolic transition	Surgical stress, high-dose steroids, insulin resistance, negative nitrogen balance	Hyperglycaemia, underfeeding, metabolic overload, poor wound healing	0.6–0.8 g/kg/day (gradual escalation)	45–50% kcal, low GI, avoid large boluses, structured timing	Limit saturated fats; cautious fibre use; monitor electrolytes (Mg, K)
Early (1–3 months)	Active anabolic recovery	Declining inflammation, improving insulin sensitivity, rising appetite	Sarcopenia, inadequate protein intake, glycaemic variability	1.0–1.2 g/kg/day	Balanced intake with even carbohydrate distribution; mixed meals	Gradual fibre increase; ensure micronutrient adequacy
Intermediate (3–12 months)	Appetite surge with metabolic stabilization	Reduced steroids, improved graft function, increased caloric intake	Weight gain, visceral adiposity, dyslipidaemia	~1.0 g/kg/day (adjusted to activity)	Emphasize complex carbohydrates, limit refined sugars	Increase unsaturated fats (MUFA/PUFA); optimize lipid profile
Long-term (>1 year)	Metabolic steady state	Stable graft function, chronic immunosuppression effects, long-term CV risk	Cardiovascular disease, metabolic syndrome, obesity	Individualised (0.8–1.0 g/kg/day)	Mediterranean-style pattern, low GI, high fibre	Emphasise heart-healthy fats, sodium restriction, micronutrient balance

Mg- Magnesium, K- Potassium, GI- Gastrointestinal, CV- Cardiovascular, MUFA- Monounsaturated fatty acids, PUFA- Polyunsaturated fatty acids

Early Recovery Phase (1–3 Months)

During the early recovery phase, declining inflammation, tapering steroids, and improving mobility facilitate a shift toward anabolic restoration. Nutritional goals focus on rebuilding lean body mass, improving insulin sensitivity, and normalizing energy intake while avoiding excess fat gain.[5,6] Protein intake should be increased to approximately 1.0–1.2 g/kg/day, emphasizing high biological value sources to support muscle synthesis and recovery.[13] Dietary fibre can be gradually introduced, and meals should include balanced macronutrients to stabilize glycaemia. Importantly, integrating nutrition with early rehabilitation, particularly resistance exercise, enhances muscle function, mitochondrial activity, and glucose uptake, making this phase critical for restoring metabolic resilience.[15,16]

Intermediate Phase (3–12 Months)

During the intermediate phase, improving appetite and reduced corticosteroid exposure support metabolic stabilization but also increase the risk of weight gain, visceral adiposity, and dyslipidaemia.[5-9] Nutritional strategies should therefore focus on maintaining metabolic flexibility while preventing excess fat accumulation. Emphasis should be placed on balanced caloric intake, avoidance of refined carbohydrates, and optimization of lipid profiles. Adoption of Mediterranean-style dietary patterns, rich in unsaturated fats, plant-based proteins, and complex carbohydrates, has been associated with improved cardiometabolic outcomes and may be particularly beneficial in this phase.[5,17]

Long-Term Maintenance (>1 Year)

In the long-term phase, transplant outcomes are largely determined by cardiovascular and metabolic health rather than graft function alone. Nutritional strategies should focus on maintaining weight stability, ensuring adequate but not excessive protein intake, moderating sodium consumption, and prioritizing high-quality fats to support cardiometabolic balance.[5,6] These dietary measures should be complemented by sustained physical activity to preserve functional capacity and metabolic fitness.[15] Increasingly, precision nutrition approaches, guided by individual metabolic risk profiles, are emerging as key tools to optimize long-term outcomes and promote durable post-transplant health.

Immunosuppression-Nutrition Interactions

Immunosuppressive therapies are central to graft survival but exert significant metabolic effects that directly influence nutritional needs and outcomes[3] (Table 2). These agents variably affect glucose metabolism, protein turnover, lipid profile, and micronutrient balance, often predisposing recipients to hyperglycaemia, sarcopenia, dyslipidaemia, and gastrointestinal intolerance. Therefore, nutritional strategies must be individualized and aligned with the specific immunosuppressive regimen to mitigate iatrogenic metabolic complications.[3,5] A coordinated, multidisciplinary approach integrating pharmacologic adjustments with targetted nutritional interventions is essential to optimize both graft function and long-term metabolic health.

Transplant Rehabilitation: Exercise, Weight, and Lipid Reprogramming

Nutrition alone is insufficient to restore metabolic health after transplantation and must be integrated with a structured rehabilitation strategy. Early mobilization is essential to counteract the effects of prolonged pre-transplant inactivity and postoperative deconditioning, followed by the gradual introduction of progressive resistance training to rebuild muscle mass and functional capacity.[19] Close monitoring of weight trajectory is critical to prevent excessive weight gain and visceral adiposity, while targetted lipid optimization helps mitigate emerging cardiovascular risk associated with immunosuppressive therapy. Skeletal muscle plays a central role in glucose disposal and metabolic regulation. Therefore, preservation and restoration of lean body mass through combined nutritional and exercise interventions are fundamental to

Table-2: Immunosuppression–Nutrition Interactions in Transplant Recipients.

Drug	Major Metabolic Effects	Mechanism	Nutritional Implications	Practical Dietary Strategies
Corticosteroids	Hyperglycaemia, increased appetite, muscle proteolysis, central adiposity	↑ Hepatic gluconeogenesis, ↑ insulin resistance, ↑ protein catabolism	Risk of postprandial glucose spikes and sarcopenia	Moderate carbohydrate intake (low GI), distribute carbs evenly; prioritize high-quality protein; avoid refined sugars
Calcineurin Inhibitors (CNI)	Impaired insulin secretion, hyperglycaemia, Mg wasting, nephrotoxicity	β-cell toxicity, ↓ insulin release, renal Mg loss	Increased risk of dysglycaemia and micronutrient deficiency	Monitor glucose closely; ensure Mg-rich foods (nuts, legumes); maintain balanced macronutrients
mTOR Inhibitors	Dyslipidaemia, hypertriglyceridaemia, impaired wound healing	Altered lipid metabolism, ↓ protein synthesis pathways	Elevated cardiovascular risk, delayed recovery	Emphasize unsaturated fats (MUFA/PUFA), limit saturated fats; avoid excess calories; ensure adequate protein for healing
Antimetabolites	GI intolerance (nausea, diarrhea), reduced intake	Mucosal irritation, altered gut turnover	Risk of inadequate caloric and protein intake	Small, frequent meals; easily digestible foods; maintain protein intake despite GI symptoms

CNI- calcineurin inhibitors, mTOR- mechanistic target of rapamycin, GI- gastrointestinal, Mg- magnesium, MUFA- monounsaturated fatty acids, PUFA- polyunsaturated fatty acids

preventing post-transplant metabolic complications and improving long-term outcomes.[19,20]

Conclusions:

Nutrition in transplant recipients must be approached as a dynamic, phase-specific intervention rather than a uniform prescription. The Nutrition Recalibration model underscores the need to align dietary progression with metabolic recovery, particularly acknowledging the early mismatch between appetite and metabolic demand. Moderated carbohydrate intake, high-quality protein, balanced amino acids, and structured rehabilitation together support lean mass preservation, improve insulin sensitivity, and mitigate cardiometabolic risk. Close integration of nutrition with immunosuppressive therapy further enhances graft stability and long-term outcomes. Ultimately, anticipatory and precision-based nutritional care can help shift transplant success from survival alone toward sustained metabolic health.

References

1. Li X, Ding R, Cai J. Organ Transplantation: Current Status, Challenges, and Future Prospects. MedComm 2026;7:e70567.
2. Chan SY, Lee J, Karki P, Laryea M, Huang J, Lim N, et al. Metabolic syndrome after liver transplantation: A silent threat to long-term success. World J Gastrointest Pharmacol Ther. 2025;16:111073. doi: 10.4292/wjgpt.v16.i4.111073. PMID: 41378074; PMCID: PMC12686996.
3. Bamgbola O. Metabolic consequences of modern immunosuppressive agents in solid organ transplantation. Ther Adv Endocrinol Metab. 2016;7:110-27.
4. ter Wee PM. Protein energy wasting and transplantation. J Ren Nutr. 2013 ;23:246-9.
5. Górska M, Kurnatowska I. Nutrition Disturbances and Metabolic Complications in Kidney Transplant Recipients: Etiology, Methods of Assessment and Prevention-A Review. Nutrients. 2022;14:4996. doi: 10.3390/nu14234996. PMID: 36501026; PMCID: PMC9738485.
6. Nolte Fong JV, Moore LW. Nutrition Trends in Kidney Transplant Recipients: the Importance of Dietary Monitoring and Need for Evidence-Based Recommendations. Front Med (Lausanne). 2018;5:302. doi: 10.3389/fmed.2018.00302. PMID: 30430111; PMCID: PMC6220714.
7. Cohen E, Korah M, Callender G, Belfort de Aguiar R, Haakinson D. Metabolic Disorders with Kidney Transplant. Clin J Am Soc Nephrol. 2020;15:732-742.
8. Tantisattamo E, Ho BT, Workeneh BT. Editorial: Metabolic Changes After Kidney Transplantation. Front Med (Lausanne). 2021;8:709644.
9. Gadwal S, Madipalli RT, Sharma S, Raju SB. Obesity in renal transplantation. Indian J Transplant. 2024;18:3–8.
10. Giusto M, Lattanzi B, Di Gregorio V, Giannelli V, Lucidi C, Merli M. Changes in nutritional status after liver transplantation. World J Gastroenterol. 2014 ;20:10682-90.
11. Arshad MT, Ali MKM, Awlqadr FH, Maqsood S, Ikram A, Hossain MS, et al. Mitigation of Metabolic Diseases Through Personalized Nutrition: A Critical In-Depth Review. Food Sci Nutr. 2026;14:e71387.
12. Giuntini EB, Sardá FAH, de Menezes EW. The Effects of Soluble Dietary Fibers on Glycemic Response: An Overview and Futures Perspectives. Foods. 2022 ;11:3934. doi: 10.3390/foods11233934. PMID: 36496742; PMCID: PMC9736284.
13. Escobedo-Monge MF, Parodi-Román J, Escobedo-Monge MA, Marugán-Miguelsanz JM. The Biological Value of Proteins for Pediatric Growth and Development: A Narrative Review. Nutrients. 2025;17:2221. doi: 10.3390/nu17132221. PMID: 40647326; PMCID: PMC12252045.
14. Dimou A, Tsimihodimos V, Bairaktari E. The Critical Role of the Branched Chain Amino Acids (BCAAs) Catabolism-Regulating Enzymes, Branched-Chain Aminotransferase (BCAT) and Branched-Chain α-Keto Acid Dehydrogenase (BCKD), in Human Pathophysiology. Int J Mol Sci. 2022;23:4022.
15. Paquin J, Tremblay R, Islam H, Riesco E, Marcotte-Chénard A, Dionne IJ. Resistance training, skeletal muscle hypertrophy, and glucose homeostasis: how related are they? A Systematic review and Meta-analysis. Appl Physiol Nutr Metab. 2024;49:1622-1635.
16. Ramos-Jiménez A, Rubio-Valles M, Ramos-Hernández JA, González-Rodríguez E, Moreno-Brito V. Adaptations in Mitochondrial Function Induced by Exercise: A Therapeutic Route for Treatment-Resistant Depression. Int J Mol Sci. 2025;26:8697. doi: 10.3390/ijms26178697. PMID: 40943622; PMCID: PMC12429612.
17. Tosti V, Bertozzi B, Fontana L. Health Benefits of the Mediterranean Diet: Metabolic and Molecular Mechanisms. J Gerontol A Biol Sci Med Sci. 2018 ;73:318-326.
18. Ravaioli F, De Maria N, Di Marco L, Pivetti A, Casciola R, Ceraso C, et al. From Listing to Recovery: A Review of Nutritional Status Assessment and Management in Liver Transplant Patients. Nutrients. 2023;15:2778. doi: 10.3390/nu15122778. PMID: 37375682; PMCID: PMC10301963.
19. De Smet S, Van Craenenbroeck AH. Exercise training in patients after kidney transplantation. Clin Kidney J. 2021;14(Suppl 2):ii15-ii24.
20. Merz KE, Thurmond DC. Role of Skeletal Muscle in Insulin Resistance and Glucose Uptake. Compr Physiol. 2020;10:785-809.