Composite and Multivisceral Transplantation

Nomenclature, Surgical Techniques, Current Practice, and Long-term Outcome

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KEYWORDS

- Liver-intestinal transplantation • Multivisceral transplantation
- Visceral transplantation • Intestinal failure • Portomesenteric venous thrombosis
- Surgical technique

KEY POINTS

- Composite and multivisceral transplantation is a life-saving procedure for patients with combined abdominal organ and gut failure.
- The observed continual improvement in survival outcome is the result of innovative surgical techniques, novel immunosuppressive protocols, and state-of-art postoperative care.
- Reestablishment of long-term nutritional autonomy with restored quality of life and socioeconomic milestones is achievable in most survivors.
- Further progress is anticipated with better in-depth understanding of innate immunity, adaptive gut alloimmunity, allograft tolerance, and the biology of gut microbiota.

INTRODUCTION

For nearly 4 decades, the abdominal viscera was considered a forbidden organ for clinical transplantation because of the associated massive lymphoid tissue, high antigenicity, and microbial colonization.[1,2] The late 1980s witnessed successful sporadic attempts under cyclosporine-based immunosuppression.[3] However, the practical application of the procedure was only feasible after the 1989 advent of tacrolimus.[4] Despite waves of enthusiasm and disappointment, the continual

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evolution of the procedure was achievable as a result of continuous interplay between new advances in surgical techniques, immunosuppressive strategies, and postoperative management.[2,5]

Establishment of the current distinctive nomenclature has largely stemmed from the anatomic and surgical principles described with the original multivisceral transplant operation.[6–8] Elucidation of the mechanisms of allograft acceptance, along with the availability of new immunosuppressive agents, has been behind the introduction of novel immunosuppressive, immunomodulatory, and preconditioning strategies.[9,10] The cumulative increase in clinical experience with advances in molecular diagnostic techniques and the availability of new antimicrobial agents enhanced postoperative care.[1]

In 2000, the Centers for Medicare and Medicaid Services qualified intestinal and multivisceral transplantation as the standard of care for patients with irreversible gut failure who no longer can be maintained on parenteral nutrition (PN).[11] With the subsequent increase in worldwide experience, practical guidelines, including expansion of the initial indications, have evolved in recent years.[12] Despite the continual improvement in outcome, the procedure is still limited to patients with nutritional failure who no longer can be maintained on PN. In addition, most health care providers also mandate failure of gut rehabilitative efforts as a prerequisite for transplantation. However, it is imperative to emphasize that early transplantation, at centers of excellence, has been associated with many therapeutic advantages, including better survival with successful restoration of nutritional autonomy and quality of life.[5] Furthermore, halting the PN-associated native liver damage with early transplantation optimizes the deceased donor liver utilization for patients with isolated hepatic failure.

HISTORICAL EVOLUTION

Traced back to the pioneer experimental work of the 1912 Nobel Prize winner Alexis Carrel,[13] the modern history of multivisceral transplantation was assigned by the innovative experimental work and initial clinical attempts of Thomas Starzl.[14,15] In 1983, 20 years after his first successful canine multivisceral transplant, Starzl performed the first 2 multivisceral transplantations in humans with en bloc inclusion of the stomach, duodenum, pancreas, intestine, colon, and liver.[16] Both cases were children with gut and liver failure associated with short bowel syndrome, which were transplanted under cyclosporine-based immunosuppression. Although the first case died perioperatively from multisystem organ failure, the second multivisceral recipient survived more than 6 months with a fully functioning graft only to die from progressive posttransplant lymphoproliferative disease (PTLD).

In 1990, Grant and colleagues[17] published the first successful case of a lesser composite visceral allograft in humans. The combined liver-intestinal allograft was transplanted under cyclosporine-based immunosuppression using the simultaneously transplanted donor liver as an immunoprotective shield to the transplanted intestine. The replaced native liver had normal structural and synthetic functions but with antithrombin III deficiency. Ironically, FK-506, currently known as tacrolimus, was introduced in the same year by the Pittsburgh team, allowing the successful clinical transplantation of the intestine-only allograft without the need for simultaneous hepatic replacement.[18] These successful initial efforts created a wave of enthusiasm that increased the clinical feasibility and practicality of the different types of visceral transplantation. In addition, new modifications were introduced to both the donor and recipient transplant procedures.[5,11,19,20]