

INTESTINAL TRANSPLANTATION

Essay

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general surgery

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Abbreviations

ACR:	Acute Cellular Rejection.
AIDS:	Acquired Immuno-Deficiency Syndrome.
AFP:	Alpha Feto Protein.
ALT:	Alanine transferase.
AST:	Aspartate transaminase.
ATP:	Adenosine Triphosphate.
BT:	Bacterial Translocation.
CMV:	Cytomegalovirus.
CNS:	Central Nervous System.
CSA:	Cyclosporine.
CT:	Computed Tomography.
DD:	Deceased Donor.
DNA:	Deoxyribonucleic Acid.
3-D:	Three- Dimensional.
EBV:	Epstein-Barr Virus.
ERCP:	Endoscopic Retrograde Cholangio-Pancreatography.
FAE:	Follicle Associated Epithelium.
GALT:	Gut Associated Lymphoid Tissue.
GFR:	Glomerular Filtration Rate.
GI:	Gastro Intestinal.
GT:	Gastrostomy Tube.
GGT:	Gamma Glutamyle Transferase.
GVHD:	Graft Versus Host Disease.
HIV:	Human Immunodeficiency Virus.
HLA:	Human Leukocytic Antigen.
ICA:	Ilio Colic Artery.
ICV:	Ilio Colic Vein.

ICU:	Intensive Care Unit.
IDF:	Intestinal Disease Foundation.
IFLs:	Intra Epithelial Lymphocytes.
IF:	Intestinal Failure.
IFALD:	Intestinal Failure Associated Liver Disease.
IgA:	Immuno- globulin A.
IL-2 R:	Interleukin-2 Receptors.
INR:	International Normalized Ratio.
ITx:	Intestinal Transplantation.
I-ITx:	Isolated Intestinal Transplantation.
ITR:	Intestine Transplant Registry.
IV:	Intra venous.
IVC:	Inferior Vena Cava.
JT:	Jujnostomy Tube.
LD:	Living Donor.
LDITx:	Living Donor Intestinal Transplantation.
L-ITx:	Liver- Intestine Transplantation.
LR-	Living Related- Small Bowel
SBTx:	Transplant.
MCV:	Mean Corpuscular Volume.
MLNs:	Mesenteric Lymph Node.
MMF:	Mycophenolate Mofetil.
MRA:	Magnetic Resonance Angiography.
MVT:	Multi- Visceral Transplantation.
mMVT:	Modified Multi- Visceral Transplantation.
NEC:	Necrotizing Enterocolitis.
OK3:	Orthoclone.
PACU:	Post Anesthesia Care Unit.
PCP:	Poly Cystic Carenii Pneumonia.
PCR:	Polymerase Chain Reaction.

PN:	Parenteral Nutrition.
PRA:	Panel Reactive Antibody.
PTLDs:	Post Transplant Lymphoproliferative Disorders.
PTT:	Partial Thromboplastin Time.
PV:	Portal Vein.
RAST:	Radio-allergo-sorbent.
RBCs:	Red Blood Corpuscles.
RCA:	Right Colic Artery.
RCV:	Right Colic Vein.
RNA:	Ribo Nucleic Acid.
SMA:	Superior Mesenteric Artery.
SMV:	Superior Mesenteric Vein.
TAC:	Tacrolimus.
TPN:	Total Parenteral Nutrition.
UCLA:	University of California Los Anglos.
UNOS:	United Network for Organ Sharing.
UW:	University of Wisconsin solution.
WBCs:	White Blood Cells.

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Introduction

Intestinal transplantation offers the hope of increased longevity and improved quality of life to adults and children with intestinal failure and life-threatening complications of chronic total parenteral nutrition. Intestinal transplantation is primarily a pediatric procedure; approximately two thirds of intestinal transplants have been performed in children.

Three types of surgical techniques are adapted to the need of the patients: isolated small bowel transplant, combined graft with liver and multi-visceral graft can be taken from cadavers or living donors. The evolution of intestinal transplantation has spanned over 40 years; however, clinical success was only achieved in the last decade. Between 1964 and 1972, only 8 intestinal transplants were performed, with the longest survival being 6 months [1].

Recipients were treated with intensive conventional immunosuppression, but the discouraging results of these first clinical trials were a consequence of technical complications, sepsis, and the inability of conventional immunosuppression to control rejection, which was attributed to the large quantity of lymphoid tissue and bacterial load of the intestine [2].

The introduction of cyclosporine (CsA) in 1980 increased survival with kidney, liver, and heart transplantation; however, results with intestine transplantation met with limited success [3, 4 & 5]. The introduction of TAC in 1990 improved actuarial graft and

patient survival rates following all types of intestine transplantation [6].

While 1- and 3-year graft survival was 30% and 20% respectively, before 1991, the corresponding survival rates increased to 60% and approximately 50% between 1995 and 1997. The current 1-year graft and patient survival rates for isolated and combined intestinal transplants have reached 80–90% for those patients who underwent transplantation between the years 2005 and 2007 according to the Intestinal Transplant Registry data presented in 2007 [7].

These impressive improvements in graft and patient outcome are certainly influenced by the refinement of surgical techniques, progress in post-transplant and intensive care treatment, as well as a better understanding of intestinal immunology have contributed to the reability of this procedure for a growing number of patients who are total parenteral nutrition (TPN)-dependent and have permanent intestinal failure. However, progress in immunosuppressive therapy, methods for monitoring and treating graft rejection, viral monitoring, as well as prevention and treatment of post-transplant Lymphoproliferative disease (PTLD) may have contributed even more decisively.

Nevertheless, Intestinal transplantation continues to be one of the greatest challenges in solid organ transplantation and to date remains a relatively uncommon procedure with approximately 1300 transplants performed worldwide, 60% of them in children, according to the Intestinal Transplant registry and it may soon become a preferred treatment and no longer a complementary one for intestinal failure.

AIM OF THE WORK

Is to discuss the value, outcomes and drawbacks of intestinal transplantation.

Historical perspective

The development of intestinal transplantation paralleled the development of other types of organ transplantation. The technical feasibility of the procedure has been established for a century but immunological feasibility was far more difficult to establish.

The high density of lymphoid tissue and the large mucosal surface area of the small intestine expressing class. Major histocompatibility antigens fuel the mutual intolerance between graft and host. As a hollow organ whose lumen is colonized by a multitude of bacteria and other micro-organisms, it behaves as a potent vector of infection to the host, a problem that is made worse by the precarious barrier from the lumen provided by the thin and vulnerable monolayer of mucosal epithelium. Here then is the fine balance between immunosuppression and infection that has bedeviled its transplantation and led to failure in so many early attempts [1].

Pre Cyclosporine Era

Following early transplantation attempts, deaths were most commonly a consequence of acute graft rejection and subsequent sepsis associated multiorgan failure. This scenario was not improved even with the introduction of combination therapy with azathioprine, prednisolone, and antilymphocyte globulin[2].

Cyclosporine Era

The introduction of cyclosporine in 1987 by Calne and colleagues [3] both accelerated progress in solid organ transplantation and rekindled interest in intestinal grafts. Success in this new cyclosporine era led to the transition from success in animals to the first long term success in humans. The Pittsburgh group transplanted a multivisceral graft consisting of a stomach, Duodenum, pancreas, small bowel, colon, and liver into a 3-year-old

Historical perspective

girl [4]. The multivisceral allograft functioned for 6 months before the child died out of lymphoma.

In 1988 Grant and colleagues reported a patient with short gut syndrome following mesenteric infarction who had undergone combined liver and small intestine transplantation and remained alive one year after the procedure. Other groups soon reported similar experiences [5].

Even though the barrier of chronic rejection was soon evident, the achievement of medium term survival was heralded as a defining moment. Thus all five LD intestinal transplants in pre- cyclosporine and cyclosporine eras were not successful in the long term because they all lacked standardized surgical donor and recipient techniques as well as potent immunosuppressive and anti-microbial therapy.

Tacrolimus Era

The introduction of Tacrolimus in the 1990s, a potent new calcineurin inhibitor that marked the next major step in allowing clinical intestinal transplantation to become a reality. The first LD intestinal transplant in Tacrolimus era was reported by Morris et al. in 1995; a 31 years old man with desmoid tumor underwent excision of the tumor, and in the same session a small bowel transplant from his monozygotic twin[6].

After the university of Minnesota's first two technically successful LD intestinal transplant, the university of Illinois group published guidelines for a standardized technique for intestinal transplant from living donor in 1997[7]. Since then, at least 25 more LD intestinal transplants have been performed worldwide.

Historical perspective

Initially, LD intestinal transplant were performed in North America and Europe. Over time, LD intestinal transplant have also been reported in Asian countries, such as Japan, China and Korea. The Japanese was performed in Kyoto in 2 years 6 month old boy who received 100 cm of distal donor ileum [8].

LD intestinal have been reported worldwide between January 1985 and March 2005 and what's overlooked in that short bowel syndrome is not a static process and that serious TPN- associated complications, such as liver failure, lack of vascular access and recurrent infections, continue to progress and become life threatening. So it's clearly demonstrated that LD intestinal grafts are life-saving if DD graft don't become available in time or if recipient progresses to end-stage liver disease and then requires an additional liver graft.

One of the most disturbing facts of TPN dependence and associated liver failure is in fact, the high mortality on the DD waiting list [9] for that reason, LD intestinal and liver transport have been considered since 1998 but not successfully performed before 2004[10].

Elective surgery such as an LD intestinal transplant allows optimal preparation of the donor and recipient reducing the risk post operative complications. LD intestinal transplant are associated with shorter preservation times and possibly lower rates of rejection due to better HLA matching. It may also facilitate the application of immunomodulatory peritansplant strategies [11].

Early rejection was then superseded by infection as the main cause of death, indicating the need to refine the target of immunological suppression to reduce infection